

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-313**

**CHEMISTRY REVIEW(S)**

**CLARINEX-D® 12 HOUR (2.5 mg desloratadine and 120 mg pseudoephedrine sulfate)  
EXTENDED RELEASE TABLETS  
NDA 21-313**

**Summary of the Basis for the Recommended Action  
from Chemistry, Manufacturing, and Controls**

**Applicant:** Schering Corporation  
2000 Galloping Hill Rd  
Kenilworth, NJ 07033

**Indication:** Used to relieve nasal and non-nasal symptoms of seasonal allergic rhinitis including nasal congestion.

**Presentation:** Bilayer tablet (one side of the tablet is the IR layer containing desloratadine, the other side is the SR layer containing pseudoephedrine), packaged in a 100 count HDPE bottle.

**EER Status:** Acceptable 22-NOV-2005

**Consults:** EA – Categorical exclusion granted under 21 CFR §25.31(b) for desloratadine. EA not required for pseudoephedrine sulfate.  
Methods Validation – Revalidation by Agency not requested

**Original Submission:** 08-DEC-2000

**Re-submission:** 29-JUL-2005 (response to AE letter)

**Post-Approval Agreements:**

The applicant agrees to place one batch annually in the post-approval stability program.

**Drug Substances:**

Desloratadine is a long acting tricyclic histamine antagonist with selective H<sub>1</sub>-receptor histamine antagonist activity. It is a white to off-white powder that is slightly soluble in water, but very soluble in ethanol and propylene glycol. The drug substance, desloratadine, is identical in all aspects to that described in NDA 21-165 for Clarinex (desloratadine) 5mg tablets. Therefore, the chemistry, manufacturing, and controls information contained in NDA 21-165 that pertain to desloratadine drug substance are referenced as applicable to NDA 21-313.

Pseudoephedrine sulphate is a synthetic salt of one of the naturally-occurring dextrorotary diastereomers of ephedrine. It is an orally-active, indirect sympathomimetic amine that exerts a decongestant action on the nasal mucosa. It is a colorless hygroscopic crystal or white, hygroscopic crystalline powder that is very soluble in water, freely soluble in alcohol, and sparingly soluble in ether. The drug substance, pseudoephedrine sulfate, is identical in all aspects to that

described in NDA 21-605 for Clarinex D-24 Hour Tablets. Therefore, appropriate reference is made to all chemistry, manufacturing, and controls information contained in NDA 21-605 that pertain to pseudoephedrine sulfate, including the further reference therein to \_\_\_\_\_, for NDA 21-313.

**Conclusion:** Drug substances are acceptable.

**Drug Product:**

The drug product, Clarinex-D® 12 hour (2.5 mg desloratadine and 120 mg pseudoephedrine sulfate) extended release tablets, described in this NDA is an oval, bilayer, uncoated tablet with a blue layer/side and a white layer/side. The blue layer is debossed with "D12". The blue immediate-release (IR) layer contains 2.5 mg of desloratadine and the white sustained-release (SR) layer contains 120 mg of pseudoephedrine sulfate. In response to the 26 October 2001 approvable letter, the sponsor has reformulated the drug product to obtain better drug product stability. The sustained release layer contains hypromellose \_\_\_\_\_ USP, as a \_\_\_\_\_. The proposed storage is at 25°C (room temperature). Submitted stability data support the proposed expiry dating of \_\_\_\_\_ for drug product packaged in the proposed bottle and \_\_\_\_\_ for drug product packaged in the proposed \_\_\_\_\_.

**Conclusion:** Drug product is satisfactory.

**Additional Items:**

The applicant has adequately responded to all deficiencies noted in the 26 October 2001 approvable letter.

Adequate stability data were provided to support the proposed expiration dating of \_\_\_\_\_ for drug product packaged in the proposed bottle and \_\_\_\_\_ for drug product packaged in the proposed blister physician sample.

All associated Drug Master Files (DMFs) are acceptable or the pertinent information has been adequately provided in the application.

A satisfactory response to the CMC labeling comments is pending.

**Overall Conclusion:**

From a CMC perspective, the application is recommended for approval, pending a satisfactory response to the labeling comments.

Blair A. Fraser, Ph.D.  
Branch Chief, Branch II  
DPA I/ONDQA

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**NDA 21-313**

**CLARINEX-D® 12 HOUR  
(2.5 mg desloratadine and 120 mg pseudoephedrine sulfate)  
EXTENDED RELEASE TABLETS**

**Shering Corporation Inc.**

**Elsbeth Chikhale, Ph.D.  
ONDQA, DPA 1, Branch 2  
for  
Division of Pulmonary and Allergy Drug Products**



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# Chemistry Review Data Sheet

1. NDA 21-313
2. REVIEW #: 2
3. REVIEW DATE: 13-JAN-2006
4. REVIEWER: Elsbeth Chikhale, Ph.D.
5. PREVIOUS DOCUMENTS: NA

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Amendment to original <sup>1</sup>	29-JUL-2005
Amendment to original <sup>2</sup>	3-OCT-2005
Amendment to original <sup>3</sup>	6-JAN-2005

- 1) The 7/29/05 amendment provides for a complete response to approvable letter dated 10/26/01
- 2) The 10/3/05 amendment provides for SAS Transfer files of the Regression Analysis as requested by the original chemistry reviewer, Prasad Peri, Ph.D. on 9/29/05.
- 3) The 1/6/06 amendment provides for a response to a (telephone) IR request dated 1/3/06.

7. NAME & ADDRESS OF APPLICANT:

Name: Schering Corporation.

Address: 200 Galloping Hill Rd  
Kenilworth, New Jersey 07033

Representative: Beth J. DiDomenico (Senior Manager and Liaison, Global  
Regulatory Affairs)

Telephone: (908) 740-2243

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Clarinex-D 12 HOUR Extended Release Tablet
- b) Non-Proprietary Name (USAN): Desloratadine/pseudoephedrine sulfate tablet
- c) Code Name/#:
- d) Chem. Type/Submission Priority:
  - Chem. Type: 14 (new molecular entity and new combination)
  - Submission Priority: S



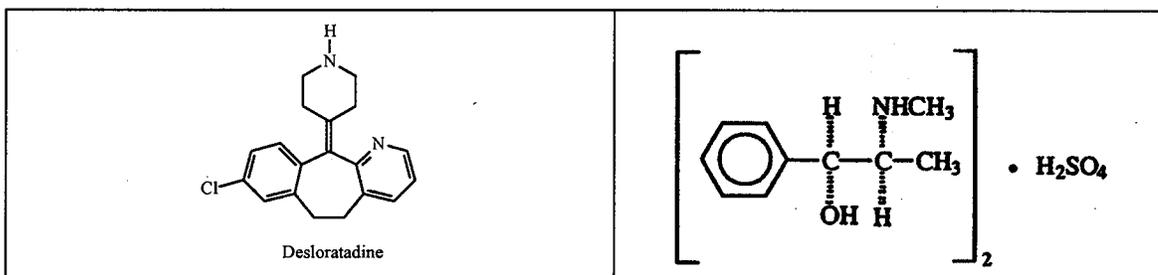
# CHEMISTRY REVIEW



## Chemistry Review Data Sheet

9. LEGAL BASIS FOR SUBMISSION: 505 (b)(2)
10. PHARMACOL. CATEGORY:  
Antihistamine/decongestant
11. DOSAGE FORM: Extended Release Tablet
12. STRENGTH/POTENCY: 2.5 mg desloratadine/tablet and 120 mg pseudoephedrine/tablet
13. ROUTE OF ADMINISTRATION: oral
14. Rx/OTC DISPENSED:  Rx  OTC
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):  
 SPOTS product  Form Completed  
 Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:



8-chloro-6,11-dihydro-11-(4-piperidinylidene)-5H-benzo[5,6]cyclohepta[1,2-b]pyridine  
Molecular Formula:  $C_{19}H_{19}ClN_2$   
Molecular Weight: 310.8

Pseudoephedrine  $H_2SO_4$ -(1S,2S)-2-methylamino-1-phenyl-1-propanol sulfate (2:1) salt  
Molecular Formula:  $(C_{10}H_{15}NO)_2 \cdot H_2SO_4$   
Molecular Weight: \_\_\_\_\_



# CHEMISTRY REVIEW



## Chemistry Review Data Sheet

### 17. RELATED/SUPPORTING DOCUMENTS:

#### A. DMFs:

DMF No.	Holder Name	Subject	LOA Date	Code <sup>1</sup>	Status <sup>2</sup> / Review Date	Reviewed By and for
[REDACTED]	[REDACTED]	[REDACTED]	2/2/05	3	Adequate 5/7/99	R. Harapanhalli for solid oral dosage form
[REDACTED]	[REDACTED]	[REDACTED]	10/6/04	3	Adequate 5/4/99	R. Harapanhalli for solid oral dosage form
[REDACTED]	[REDACTED]	[REDACTED]	2/1/05	3	Adequate 3/24/00	D. Klein for solid oral dosage form
[REDACTED]	[REDACTED]	[REDACTED]	3/28/05	4	N/A	
[REDACTED]	[REDACTED]	[REDACTED]	2/1/05	3	Adequate 3/20/1999	H. Khorshidi for solid oral dosage form.
[REDACTED]	[REDACTED]	[REDACTED]	9/27/04	3	Adequate 8/11/00	R. Trimmer for solid-oral dosage form
[REDACTED]	[REDACTED]	[REDACTED]	10/6/04	3	[REDACTED] Adequate (S/Z/S/R/D)	K. Swiss for Tablets
[REDACTED]	[REDACTED]	[REDACTED]			[REDACTED] Adequate	P. Peri for Tablets

<sup>1</sup> Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no relevant revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

<sup>2</sup> Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)



# CHEMISTRY REVIEW



## Chemistry Review Data Sheet

### B. Other Documents:

Type	Number	Owner	Subject
IND	59,109	Schering Corp.	Desloratadine Reditabs
IND			
IND	58,545	Schering Plough	Desloratadine SCH-483-QD and Pseudoephedrine
IND	58,506	Schering Plough	Desloratadine SCH-483-BID and Pseudoephedrine
IND	57,960	Schering Corp	Desloratadine Syrup
IND	55,364	Schering Plough	SCH 34117 Tablets
NDA	19-658	Schering Corp.	Claritin® (Loratadine) 10 mg Tablet
NDA	19-670	Schering Corp.	Claritin® D-12 Hour (5 mg Loratadine/ 120 mg pseudoephedrine sulfate)
NDA	21-165	Schering Plough	Desloratadine 5 mg Tablets
NDA	21-312	Schering	Clarinet Reditabs,
NDA	21-300	Schering	Clarinet Syrup
NDA	21-605	Schering	Clarinet-D 24 Hour (5 mg Desloratadine/ 240 mg pseudoephedrine sulfate)
NDA	21-297	Alternate indication for NDA 21-165	

### 18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A		
EES	Acceptable	11/22/05	Elsbeth Chikhale, Ph.D.
Pharm/Tox	N/A		
Clinical Pharmacology and Biopharmaceutics	Acceptable	1/10/06	Sayed Al Habet, Ph.D.
Methods Validation	Acceptable	12/8/05	John Hill, Ph.D.
ODS	N/A		
EA	Satisfactory (consult not needed)	1/13/06	Elsbeth Chikhale, Ph.D.
Microbiology	N/A		
Labeling		1/13/06	Prasad Peri, Ph.D.

### 19. ORDER OF REVIEW: N/A



# The Chemistry Review for NDA 21-313

## The Executive Summary

### I. Recommendations

#### A. Recommendation and Conclusion on Approvability

NDA 21-313 is recommended for **approval** from the standpoint of chemistry, manufacture and controls, pending a response to the labeling comments and evaluation of the response by Prasad Peri, Ph.D. The submitted stability data support an **expiration date** of \_\_\_\_\_ for drug product packaged in the proposed bottle and \_\_\_\_\_ for drug product packaged in the proposed \_\_\_\_\_.

#### B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

None

### II. Summary of Chemistry Assessments

#### A. Description of the Drug Product(s) and Drug Substance(s)

##### 1) Drug Product

The drug product, Clarinex-D® 12 hour (2.5 mg desloratadine and 120 mg pseudoephedrine sulfate) extended release tablets, described in this NDA is an oval bilayer \_\_\_\_\_ tablet with a blue layer/side and a white layer/side. The blue layer is debossed with "D12". The blue immediate-release (IR) layer contains 2.5 mg of desloratadine and the white sustained-release (SR) layer contains 120 mg of pseudoephedrine sulfate. In response to the 10/26/01 approvable letter, the sponsor has reformulated the drug product to obtain better drug product stability. The sustained release layer contains hypromellose \_\_\_\_\_ USP as \_\_\_\_\_.

The drug product has a blue side and a white side (bilayer), in contrast to the previously approved drug product, Clarinex-D® 24 hour (5 mg desloratadine and 240 mg pseudoephedrine sulfate) extended release tablets (NDA 21-605), which has a \_\_\_\_\_. Also, several of the excipients present in the reformulated drug product (Clarinex-D 12 hour) are different from the excipients in the Clarinex-D 24 hour tablets. The drug product is indicated for the relief of nasal and non-nasal symptoms of seasonal allergic rhinitis including nasal congestion. The proposed storage is at 25°C (room temperature). Submitted stability data support the proposed expiry dating of \_\_\_\_\_ for drug product packaged in the proposed bottle and \_\_\_\_\_ for drug product packaged in the proposed \_\_\_\_\_.

##### 2) Drug Substance

Desloratadine is a long acting tricyclic histamine antagonist with selective H1-receptor histamine antagonist activity. It is a white to off-white powder that is slightly soluble in water, but very soluble in ethanol and propylene glycol. The drug substance, desloratadine, is identical in all aspects to that described in NDA 21-165 for Clarinex (desloratadine) 5mg tablets. Therefore, the chemistry, manufacturing, and controls information contained in NDA 21-165 that pertain to desloratadine drug substance are referenced as applicable to NDA 21-313.

Pseudoephedrine sulphate is a synthetic salt of one of the naturally occurring dextrorotary diastereomer of ephedrine. It is an orally active indirect sympathomimetic amine that exerts a decongestant action on the nasal mucosa. It is a colorless hygroscopic crystal or white,



hygroscopic crystalline powder that is very soluble in water, freely soluble in alcohol, and sparingly soluble in ether. The drug substance, pseudoephedrine sulfate, is identical in all aspects to that described in NDA 21-605 for Clarinex D-24 Hour Tablets. Therefore, appropriate reference is made to all chemistry, manufacturing, and controls information contained in NDA 21-605 that pertain to pseudoephedrine sulfate, including the further reference therein to \_\_\_\_\_ Type II DMF \_\_\_\_\_ for NDA 21-313.

**B. Description of How the Drug Product is Intended to be Used**

The drug product is an extended release tablet intended for twice daily dosing. Submitted stability data support the proposed expiry date of \_\_\_\_\_ for drug product packaged in the proposed bottle and \_\_\_\_\_ for drug product packaged in the proposed \_\_\_\_\_

**C. Basis for Approvability or Not-Approval Recommendation**

This NDA is recommended for approval because:

- The applicant has adequately responded to all deficiencies noted in the 10/26/01 approvable letter.
- The applicant has demonstrated that the manufacturing of the drug product is adequately controlled and assures a consistent high quality drug product.
- Adequate stability data were provided to support the proposed expiration dating of \_\_\_\_\_ for drug product packaged in the proposed bottle and \_\_\_\_\_ for drug product packaged in the proposed \_\_\_\_\_

**III. Administrative**

**A. Reviewer's Signature**

\_\_\_\_\_  
**Elsbeth Chikhale, Ph.D.**

**B. Endorsement Block:** in DFS

**C. cc Block:** in DFS

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Blair Fraser  
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CHEMIST

## Memorandum

**Date:** 08-DEC-2005  
**Assignment received:** 18-NOV-2005  
**From:** John Hill, Ph.D., Review Chemist, Branch II/DPA I/ONDQA  
**To:** Elsbeth Chikhale  
**Re:** **NDA 21-313**  
**Clarinex-D 12 Hour (2.5mg desloratadine and 120mg pseudoephedrine sulfate)**  
**Extended Release Tablet**  
Letter date: 29-JUL-2005  
(Complete Response to the 26-OCT-2001 Approvable letter)  
**Subject:** **NDA Method Validation Assessment**

### Overall Conclusion:

The applicant has adequately addressed the prior AE deficiencies. In support of the new drug product formulation, all test methods have been re-validated for their intended purposes. The included method validation data are scientifically sound. There are no outstanding CMC issues concerning the validation of the test methods.

### AE Deficiencies and Answers:

The original NDA was reviewed and found deficient from a CMC viewpoint. An AE letter was issued, based on the chemistry review, on 26-OCT-2001. A complete response to this AE letter was submitted on 29-JUL-2005. The following questions pertaining to method validation were included in the AE letter:

5. The following comments pertain to the drug product method for appearance.

5.a. Provide results for the \_\_\_\_\_ values of the reference standards.

**Response:** The Reviewer is referred to Section 3.2.P.5.3.9 "Validation of Analytical Procedures", specifically to validation of the method "Color Determination Using Spectrophotometer", specifically to the table listing entitled "Summary of System Suitability Results" for the requested values.

5.b. Provide details (including validation) for determining the quantitative description of color for the tablets.

**Response:** b. The Reviewer is referred to Amendment Quality Section 3.2.P.5.2 where the spectrophotometric method for examination of drug product color is described and to Section 3.2.P.5.3.9 for its validation.

**Review Comment:** The requested action(s)/data are addressed in section 3.2.P.5.3.9, "Method Evaluation and Validation Report for Color Determination of Clarinex D-12 and Clarinex Plus Tablets Using Spectrophotometer". These method validation data and reports have been reviewed and are suitable. The validation report fully addresses the deficiencies raised in the AE letter. The applicant has appropriately validated this method for its intended purpose.

6. The following comments pertain to the dissolution method and detection by HPLC and UV analysis.

6.a. Provide additional validation data for the alternate quantitation method that utilizes the \_\_\_\_\_ column maintained at \_\_\_\_\_. You are reminded that only validated columns be listed in the methods.

**Response:** a. The Reviewer is referred to Section 3.2.P.5.3.1 .Validation of Analytical Procedures, with specific reference to validation of the HPLC quantitation method for dissolution testing. The validation provided therein establishes the suitability of the HPLC method.

6.b. Provide for the robustness of the HPLC quantitation method by changing suitable parameters (e.g.,

**Response:** With reference to the COMMENT 6.a. response above, validation of the HPLC quantitation method as described in Section 3.2.P.5.3 adequately addresses the method's robustness with respect to reasonable variations for the listed parameters.

6. e. Adopt the HPLC method as the regulatory method, since the UV method cannot distinguish between the actives and impurities and degradation products. (Refer to COMMENT 13.e. below).

**Response:** The Reviewer is referred to Section 3.2.P.5.2 "Analytical Procedures" and to Section 3.2.P.5.3 "Validation of Analytical Procedures" as they pertain to Dissolution Testing. The respective methods are described and sufficiently validated as suitable for their intended use. Accordingly, the Reviewer's concern for the UV method should be addressed. Although the HPLC Method is designated in Section 3.2.P.5.1, "Specifications" as the "Regulatory Method", either analytical method may be used for Dissolution Testing.

6.f. Provide system suitability requirements for the UV test method and adequate validation data for accuracy of the UV method.

**Response:** Per response to COMMENT 6.e., adequate system suitability control is provided to ensure the reliability of the method. The system suitability described is supported by validation of the method as described in Section 3.2.P.5.3.

**Review Comment:** The requested action(s)/data are addressed in section 3.2.P.5.3.1, "Method Validation Report for the Determination of Dissolution Release of Desloratadine and Pseudoephedrine Sulfate in SCH 483 Desloratadine-PSE (2.5 mg DL/120 mg PSE) Tablets by HPLC (Investigation Phase and Registration Phase)" and section 3.2.P.5.3, "Method Validation Report for the Determination of Desloratadine and Related Substances in SCH 483 Desloratadine-PSE (2.5 mg DL/120 mg PSE) Tablets by HPLC (Investigation Phase and Registration Phase)". These method validation data and reports have been reviewed and are suitable. The validation reports submitted in the complete response fully addresses the deficiencies raised in the AE letter. The applicant has appropriately validated these methods for their intended purpose.

8. The following comments pertain to the HPLC Procedure for Identification, Assay, Content Uniformity, and Degradation Products for Pseudoephedrine Sulfate in Clarinex-D 12 Hour Tablets (Method # 000483-126A-021-02.01).

8. a. From the data provided in section 4.B.6, page 300, monitoring the degradants at dual wavelengths (                      ), will provide the best estimate of the amounts of degradants present in the drug product. Provide an updated method that incorporates these changes.

**Response:** Although the method stated in the above referenced Amended Quality Section is a different one, it is similar to that in COMMENT and merits response. While it is acknowledged that the suggested dual wavelength approach would theoretically provide satisfactory results, the method as described in Amended Quality Section 3.2.P.5.2. satisfactorily fulfills all criteria necessary to serve its intended purpose. The Reviewer is referred to Amendment Quality Section 3.2.P.5.3.4 describing the validation of this method for assurance of its capability.

8. b. Provide a description of the elution of desloratadine and its degradants present in the tablets while using the proposed HPLC method. Clarify how they are separated from the pseudoephedrine degradants.

**Response:** Elution of desloratadine and/or any of its degradants occur(s) much later, of the order of many hours and will not interfere with pseudoephedrine or any of its degradants. The Reviewer is referred to Amendment Quality Section 3.2.P.5.3.4 describing validation of this method, particularly to the discussion entitled "Specificity- Stressed Conditions" where it is shown that tablets were stressed, analyzed and UV spectra of peaks obtained to show that there is no interference.

**Review Comment:** The requested action(s)/data are addressed in section 3.2.P.5.3.4, "Method Validation Report for the Determination of Pseudoephedrine Sulfate and Related Substances in SCH 483 Desloratadine-PSE (2.5 mg DL/120 mg PSE) Tablets by HPLC (Investigation Phase and Registration Phase)". The validation report fully addresses the deficiencies raised in the AE letter. These method validation data and reports have been reviewed and are suitable. The applicant has appropriately validated this method for its intended purpose.

10. The following comments pertain to the Determination of Residual [redacted] in Desloratadine Tablets by [redacted]

10. a. Provide a listing of all equivalent columns proposed for the [redacted] analysis of [redacted]

**Response:** a. The method in COMMENT specifies a single column for use. As shown within the validation of the method presented in Section 3.2.P.5.3.8 three (3) different columns of the same description and manufacturer representing differing manufacturing lots produced satisfactory performance. In the event future plans call for the use of alternate columns, the sponsor recognizes its responsibility to provide such in an appropriate regulatory submission along with comparability data supportive of suitable performance capability.

**Review Comment:** The requested action(s)/data are addressed in section 3.2.P.5.3.8, "Method Validation Report for the Determination of Residual Solvents [redacted] in SCH 483 Desloratadine-PSE (2.5 mg DL/120 mg PSE) Tablets by [redacted] (Investigation Phase and Registration Phase)". The method has been validated for use with several similar chromatographic columns. These method validation data and reports have been reviewed and are suitable. The applicant has appropriately validated this method for its intended purpose.

17. Provide a sample chromatogram of a mixture of degradants and representative chromatograms from stability studies, showing quantifiable separation of peaks as indicated in the reported stability results (e.g., RRT 0.69 and RRT 0.70).

**Response:** The Reviewer is referred to Amended Quality Section 3.2.P.5.3 . Validation of Analytical Methods. for Validation of the method used for desloratadine degradation products. Attachment 6, therein is a chromatogram showing elution of degradation products in the presence of desloratadine. For pseudoephedrine sulfate, reference is made to Section 3.2.P.5.3 . Validation of Analytical Methods, pertaining to the HPLC method for pseudoephedrine sulfate degradation products. Attachment 5 provides chromatograms of sample preparations for tablets subjected to heat and light stress and shows elution of degradants in the presence of pseudoephedrine. The specific request with reference to the relative retention times mentioned in the Comment is no longer relevant since the method from which it was derived is not described in this submission.

**Review Comment:** The requested action(s)/data are addressed in section 3.2.P.5.3.4, "Method Validation Report for the Determination of Pseudoephedrine Sulfate and Related Substances in SCH 483 Desloratadine-PSE (2.5 mg DL/120 mg PSE) Tablets by HPLC (Investigation Phase and Registration Phase)". The validation report fully addresses the deficiencies raised in the AE letter and contains the requested HPLC profiles. These method validation data, chromatograms and

reports have been reviewed and are suitable. The applicant has appropriately validated this method for its intended purpose.

**Analytical Methods:**

Appropriate tests, methods and acceptance criteria have been selected to assure the identity, purity, physical, and microbial properties of a bilayer tablet. These release tests and specifications are summarized in the following table.

**Release Tests and Specifications**

Test Method	Release Specification	Schering-Plow Procedure #
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**DIVISION OF PULMONARY AND ALLERGY DRUG PRODUCTS**  
**Review of Chemistry, Manufacturing, and Controls**

NDA #:21-313

CHEM. REVIEW #: 1REVIEW DATE: 8/3/01RECOMMEND ACTION: NOT APPROVABLE

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL N000	12/08/00	12/11/00	1/09/01
Amendment N000BC	3/26/01	3/28/01	4/6/01
Amendment N000BZ	4/27/01	4/30/01	4/30/01
Amendment N000WA	5/22/01	5/23/01	5/23/01

NAME & ADDRESS OF APPLICANT:

Schering Corporation  
 2000 Galloping Hill Road  
 Kenilworth, NJ 07033

DRUG PRODUCT NAME:Proprietary:

Clarinet-D™ 12 Hour Extended-release Tablet

Nonproprietary/USAN:

Desloratidine Tablet

Code Name/#:

SCH 483

Chem. Type/Ther. Class:

1, 4S

PHARMACOL.CATEGORY/INDICATION:

Desloratidine is an antihistamine (peripheral H<sub>1</sub>-receptor antagonist) and pseudoephedrine sulfate is an adrenergic vasoconstrictor

DOSAGE FORM:

Blue white bilayer Extended-release Tablets

STRENGTHS:

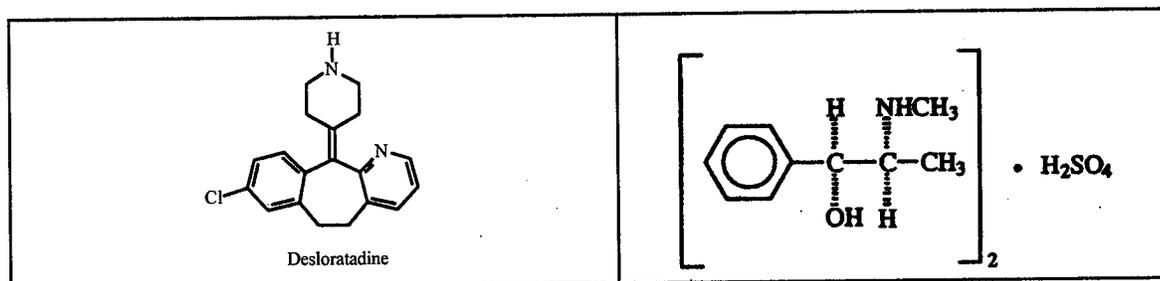
Desloratidine 2.5 mg and pseudoephedrine sulfate 120 mg

ROUTE OF ADMINISTRATION:

Oral

DISPENSED: Rx OTCSPECIAL PRODUCTS: YES NO

(If yes, fill out the form for special products and deliver to the TIA through the team leader for data entry)

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

8-chloro-6,11-dihydro-11-(4-piperidinylidene)-5H-benzo[5,6]cyclohepta[1,2-b]pyridine

Molecular Formula: C<sub>19</sub>H<sub>19</sub>ClN<sub>2</sub>

Molecular Weight: 310.8

Pseudoephedrine H<sub>2</sub>SO<sub>4</sub>-(1S,2S)-2-methylamino-1-phenyl-1-propanol sulfate (2:1) salt

Molecular Formula: (C<sub>10</sub>H<sub>15</sub>NO)<sub>2</sub>•H<sub>2</sub>SO<sub>4</sub>

Molecular Weight: \_\_\_\_\_

**SUPPORTING DOCUMENTS:**

**DMFs**

DMF No.	Holder Name	Subject	LOA Date	Status/ Review Date	Reviewed By and for	Reference in Reviews
[REDACTED]	Schering Plough Avondale Co.	[REDACTED]	NDA 21165	Adequate 11/23/99	K. Swiss for solid oral	Page 8
[REDACTED]	Schering Plough Singapore Ltd.	[REDACTED]	NDA 21165	Withdrawn 5/22/01	K. Swiss for solid oral	Page 8
[REDACTED]	[REDACTED]	[REDACTED]	7/6/99	Inadequate 2/6/01	K. Swiss for solid oral letter sent dated 2/7/01	Page 8
[REDACTED]	[REDACTED]	[REDACTED]	2/29/00	Adequate 5/7/99	R. Harapanhalli for solid oral dosage form	Page 80
[REDACTED]	[REDACTED]	[REDACTED]	2/28/00	Adequate 5/4/99	R. Harapanhalli for solid oral dosage form	Page 80
[REDACTED]	[REDACTED]	[REDACTED]	2/8/00	Adequate 3/24/00	D. Klein for solid oral dosage form	Page 80
[REDACTED]	[REDACTED]	[REDACTED]	2/25/00	Adequate 10/13/98	W. Berlin for solid oral dosage form	Page 81
[REDACTED]	[REDACTED]	[REDACTED]	5/15/00	Adequate 3/20/1999	H. Khorshidi for solid oral dosage form.	Page 81
[REDACTED]	[REDACTED]	[REDACTED]	7/31/00	Adequate 8/11/00	R. Trimmer for solid oral dosage form	Page 81
[REDACTED]	[REDACTED]	[REDACTED]	7/25/00	Adequate 8/03/01	P. Peri for solid oral dosage form.	Page 81
[REDACTED]	[REDACTED]	[REDACTED]	5/16/00	Adequate (5/23/00)	K. Swiss for Tablets	Page 81
[REDACTED]	[REDACTED]	[REDACTED]		Adequate	P. Peri for Tablets	

**RELATED DOCUMENTS (if applicable)**

Type	Number	Owner	Subject
IND	59,109	Schering Corp.	Desloratadine Reditabs
IND	[REDACTED]	[REDACTED]	[REDACTED]
IND	58,545	Schering Plough	Desloratadine SCH-483-QD and Pseudoephedrine
IND	58,506	Schering Plough	Desloratadine SCH-483-BID and Pseudoephedrine
IND	57,960	Schering Corp	Desloratadine Syrup
IND	55,364	Schering Plough	SCH 34117 Tablets
NDA	19-658	Schering Corp.	Claritin® (Loratadine) 10 mg Tablet
NDA	19-670	Schering Corp.	Claritin® D-12 Hour (5 mg Loratadine/ 120 mg pseudoephedrine sulfate)
NDA	21-165	Schering Plough	Desloratadine 5 mg Tablets
NDA	21-312	Schering	Clarinet Reditabs,
NDA	21-300	Schering	Clarinet Syrup
NDA	21-297	Alternate indication for NDA 21-165	

109 Page(s) Withheld

X § 552(b)(4) Trade Secret / Confidential

       § 552(b)(4) Draft Labeling

       § 552(b)(5) Deliberative Process