CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-605

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Department of Health and Human Services
Food and Drug Administration

Form Approved: OMB No. 0910-0513
Expiration Date: 7/31/06
See OMB Statement on Page 3.

PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT

For Each Patent That Claims a Drug Substance (Active Ingredient), Drug Product (Formulation and Composition) and/or Method of Use

NDA NUMBER: To Be Assigned

NAME OF APPLICANT / NDA HOLDER: SCHERING CORPORATION

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)
CLARINEX - D™ 24 Hour Extended Release Tablets

ACTIVE INGREDIENT(S)	STRENGTH(S)
Desloratadine Pseudoephedrine Sulfate, USP	5 mg Desloratadine 240 mg Pseudoephedrine Sulfate, USP

DOSAGE FORM
Tablets

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the *only* information relied upon by FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you submit an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number 4,659,716	b. Issue Date of Patent April 21, 1987	c. Expiration Date of Patent April 21, 2004
d. Name of Patent Owner SCHERING CORPORATION	Address *(of Patent Owner)* 2000 Galloping Hill Road City/State Kenilworth, New Jersey ZIP Code 07033-0530 FAX Number *(if available)* 908-298-5388 Telephone Number 908-298-4000 E-Mail Address *(if available)*	
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States) James R. Nelson	Address *(of agent or representative named in 1.e.)* Patent Department K-6-1 Mailstop 1990 2000 Galloping Hill Road City/State Kenilworth, New Jersey ZIP Code 07033-0530 FAX Number *(if available)* 908-298-5388 Telephone Number 908-298-2959 E-Mail Address *(if available)* james.nelson@spcorp.com	

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above? ☐ Yes ☒ No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? ☐ Yes ☐ No

FORM FDA 3542a (7/03)

SCHERING-PLOUGH RESEARCH INSTITUTE

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? See Attachment 1	☐ Yes	☒ No
2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? See Attachment 2	☐ Yes	☐ No
2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).	☐ Yes	☐ No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)	☐ Yes	☒ No
2.6 Does the patent claim only an intermediate?	☐ Yes	☒ No
2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?	☒ Yes	☐ No
3.2 Does the patent claim only an intermediate?	☐ Yes	☒ No
3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

4. Method of Use

Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?	☒ Yes	☐ No

4.2 Claim Number (*as listed in the patent*)	Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?		
14 and 15		☒ Yes	☐ No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: *(Submit indication or method of use information as identified specifically in the proposed labeling.)*
	See Attachment 3.

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.	☐ Yes

6. Declaration Certification

6.1 ***The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.***

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner *(Attorney, Agent, Representative or other Authorized Official) (Provide information below)*	Date Signed
James R Nelson	4/9/04

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

☐ NDA Applicant/Holder	☒ NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
☐ Patent Owner	☒ Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name: James R. Nelson	
Address: Schering Corporation Patent Department K-6-1 Mailstop 1990 2000 Galloping Hill Road	City/State: Kenilworth, New Jersey
ZIP Code: 07033-0530	Telephone Number: 908-298-2959
FAX Number *(if available)*: 908-298-5388	E-Mail Address *(if available)*: james.nelson@spcorp.com

The public reporting burden for this collection of information has been estimated to average 9 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Form FDA 3542a
Clarinex D™ 24 Hour Extended Release Tablets
USPN 4,659,716

ATTACHMENT 1

Item 2.1:

On August 1, 2003, the U.S. Court of Appeals for the Federal Circuit in *Schering Corp. v. Geneva Pharmaceuticals Inc., et al*, 339 F. 3rd 1373 (Fed. Cir. 2003), affirmed the Opinion and Order of the U.S. District Court for the District of New Jersey, that invalidated claims 1 and 3 of U.S. Patent No. 4,659,716 as anticipated by U.S. Patent No. 4,282,233 and also stated that claims 14-16 covering methods of treating allergic reactions were not anticipated by U.S. Patent No. 4,282,233.

At least claims 5, 7, 9, 14 and 15 of U.S. Patent No. 4,659,716 read on Clarinex-D™ 24 Hour (desloratadine and Pseudoephedrine, USP) Extended Release Tablets for the indication for which approval is sought, namely, for the relief of nasal and non-nasal symptoms of seasonal allergic rhinitis, including nasal congestion, in adults and children 12 years of age and older.

Form FDA 3542a
Clarinex D™ 24 Hour Extended Release Tablets
USPN 4,659,716

ATTACHMENT 2

Item 2.2:

Because U.S. Patent No. 4,659,716 claims the approved drug product, it qualifies for listing on that basis and thus Question 3.1 is answered affirmatively. Because U.S. Patent No. 4,659,716 does not claim the drug substance in the approved drug product *per se*, Question 2.1 is answered negatively. Accordingly, we do not address Questions 2.2, 2.3 or 2.4 on the Form concerning other forms of the drug substance.

Form FDA 3542a
Clarinex D™ 24 Hour Extended Release Tablets
USPN 4,659,716

ATTACHMENT 3

Item 4.2a:

CLARINEX-D 24 HOUR Extended Release Tablets is indicated for the relief of the nasal and non-nasal symptoms of allergic rhinitis (seasonal ————), including nasal congestion, in patients 12 years of age or older. CLARINEX-D 24 HOUR Extended Release Tablets can be administered when the antihistaminic properties of desloratadine and the nasal decongestant activity of pseudoephedrine are desired.

Appears This Way
On Original

Department of Health and Human Services
Food and Drug Administration

PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT

For Each Patent That Claims a Drug Substance (Active Ingredient), Drug Product (Formulation and Composition) and/or Method of Use

Form Approved: OMB No. 0910-0513
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NDA NUMBER
To Be Assigned

NAME OF APPLICANT / NDA HOLDER
SCHERING CORPORATION

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)
CLARINEX - D™ 24 Hour Extended Release Tablets

ACTIVE INGREDIENT(S)	STRENGTH(S)
Desloratadine Pseudoephedrine Sulfate, USP	5 mg Desloratadine 240 mg Pseudoephedrine Sulfate, USP

DOSAGE FORM
Tablets

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FDA will not list patent information if you submit an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number
6,100,274

b. Issue Date of Patent
August 8, 2000

c. Expiration Date of Patent
July 7, 2019

d. Name of Patent Owner
SCHERING CORPORATION

Address *(of Patent Owner)*
2000 Galloping Hill Road

City/State
Kenilworth, New Jersey

ZIP Code
07033-0530

FAX Number *(if available)*
908-298-5388

Telephone Number
908-298-4000

E-Mail Address *(if available)*

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

James R. Nelson

Address *(of agent or representative named in 1.e.)*
Patent Department K-6-1 Mailstop 1990 2000 Galloping Hill Road

City/State
Kenilworth, New Jersey

ZIP Code
07033-0530

FAX Number *(if available)*
908-298-5388

Telephone Number
908-298-2959

E-Mail Address *(if available)*
james.nelson@spcorp.com

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above? ☐ Yes ☒ No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? ☐ Yes ☐ No

FORM FDA 3542a (7/03)

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement?	☐ Yes	☒ No
2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? See Attachment 1	☒ Yes	☐ No
2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).	☐ Yes	☐ No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)	☐ Yes	☒ No
2.6 Does the patent claim only an intermediate?	☐ Yes	☒ No
2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?	☒ Yes	☐ No
3.2 Does the patent claim only an intermediate?	☐ Yes	☒ No
3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

4. Method of Use

Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?	☐ Yes	☒ No

4.2 Claim Number (*as listed in the patent*)	Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?	☐ Yes	☐ No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: *(Submit indication or method of use information as identified specifically in the proposed labeling.)*

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.	☐ Yes

6. Declaration Certification

6.1 ***The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.***

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6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner *(Attorney, Agent, Representative or other Authorized Official) (Provide information below)*	Date Signed

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Check applicable box and provide information below.

☐ NDA Applicant/Holder	☒ NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
☐ Patent Owner	☒ Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name James R. Nelson	
Address Schering Corporation Patent Department K-6-1 Mailstop 1990 2000 Galloping Hill Road	City/State Kenilworth, New Jersey
ZIP Code 07033-0530	Telephone Number 908-298-2959
FAX Number *(if available)* 908-298-5388	E-Mail Address *(if available)* james.nelson@spcorp.com

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Food and Drug Administration
CDER (HFD-007)
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Rockville, MD 20857

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Form FDA 3542a
Clarinex D™ 24 Hour Extended Release Tablets
USPN 6,100,274

ATTACHMENT 1

Item 2.2:

Because U.S. Patent No. 6,100,274 claims the approved drug product, it qualifies for listing on that basis and thus, Question 3.1 is answered affirmatively.
Because U.S. Patent No. 6,100,274 does not claim the drug substance in the approved drug product *per se*, Question 2.1 is answered negatively.
Accordingly, we do not address Questions 2.2, 2.3 or 2.4 on the Form concerning other forms of the drug substance.

Appears This Way
On Original

Claim for Data Exclusivity (Section 20)

1. Pursuant to the provisions of Sections 505(c)(3)(D)(iii) and 505 (j)(5)(D)(iii) of the Food, Drug and Cosmetic Act (FDCA) and 21 CFR 314.108 (b)(4)(iv), the applicant claims three (3) years of exclusivity for its CLARINEX-D 24(desloratadine, 5 mg and pseudoephedrine sulfate, 240 mg) Extended Release Tablets for the relief of nasal and non-nasal symptoms of allergic rhinitis including nasal congestion, in adults and children 12 years of age and older.

2. The applicant certifies that to the best of the applicant's knowledge each of the clinical investigations included in the application meets the definition of "new clinical investigation" set forth in 21 CFR 314.108(a).

3. A list of all published studies or publicly available reports of clinical investigations known to the applicant through a computer-assisted literature search that are relevant to the conditions for which the applicant is seeking approval is provided as **Attachment 1**.

4. The applicant certifies that it has thoroughly searched the scientific literature during the period 1980 to February 11, 2004 through a computer-assisted search of the Scholar database including the scientific and medical literature, and Dialog database encompassing the subfiles MEDLINE, BIOSIS, EMBASE, and Derwent Drug File,for English and non-English literature relating to CLARINEX-D 24 (desloratadine, 5 mg and pseudoephedrine sulfate, 240 mg) Extended Release Tablets for the relief of nasal and non-nasal symptoms of allergic rhinitis, including nasal congestion, in adults and children 12 years of age and older, covering the periods listed.

5. To the best of the applicant's knowledge, the list of scientific literature pertaining to CLARINEX-D 24 (desloratadine, 5 mg and pseudoephedrine sulfate, 240 mg) Extended Release Tablets for the relief of nasal and non-nasal symptoms of allergic rhinitis, including nasal congestion, in adults and children 12 years of age and older, without reference to the new information contained in the clinical trials in the application.

6. The applicant's opinion that the studies or reports are insufficient is based on the following: The literature does not contain adequate characterization of the efficacy and safety profile of CLARINEX-D 24 (desloratadine, 5 mg and pseudoephedrine sulfate, 240 mg) Extended Release Tablets for the relief of nasal and non-nasal symptoms of allergic rhinitis, including nasal congestion, in adults and children 12 years of age and older, which is established by the data from the new clinical studies conducted by the applicant and included in this NDA Supplement.

7. The applicant was the sponsor named in the Form FDA-1571 for IND under which the new clinical investigations were conducted.

PEDIATRIC USE

As discussed in a meeting with the Agency on November 7, 2000, the Applicant hereby requests a waiver of the requirements of 21 CFR 314.55(a) "Pediatric use information" for the pediatric age groups below the age of 12. The Applicant certifies that this drug product does not represent a meaningful therapeutic benefit over existing treatments and is not likely to be used in a substantial number of pediatric patients below the age of 12 years.

The safety of desloratadine syrup (0.5mg/mL) is currently being evaluated in children down to the age of six months. This data will be the subject of one or more NDA's and will be responsive to the Agency's formal pediatric Written Request. Pseudoephedrine, in pediatric dose form, is currently available over-the-counter. In addition, this drug product is not likely to be used in a substantial number of pediatric patients because it is uniquely designed to deliver 240 mg of pseudoephedrine from a controlled release matrix over a 24 hour period. This dose of pseudoephedrine is not recommended for patients below the age of 12.

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA # : 21-605 Supplement Type (e.g. SE5): _____ Supplement Number:

Stamp Date: May 4, 2004 PDUFA Goal Date: March 3, 2004

HFD 570 Trade and generic names/dosage form: Clarinex-D 24 Hour (deloratadine 5mg/pseudoephedrine 240mg)

Applicant: Schering Corporation Therapeutic Class: 3S

Does this application provide for new active ingredient(s), new indication(s), new dosage form, new dosing regimen, or new route of administration? *

☑ Yes. Please proceed to the next section.

☐ No. PREA does not apply. Skip to signature block.

** SE5, SE6, and SE7 submissions may also trigger PREA. If there are questions, please contact the Rosemary Addy or Grace Carmouze.*

Indication(s) previously approved (please complete this section for supplements only):
(Each indication covered by this application must have pediatric studies: Completed, Deferred, and/or Waived.)

Number of indications for this application(s): 1

Indication #1: Relief of nasal and non-nasal symptoms of seasonal allergic rhinitis.

Is this an orphan indication?

☐ Yes. PREA does not apply. Skip to signature block.

☑ No. Please proceed to the next question.

Is there a full waiver for this indication (check one)?

Yes: Please proceed to Section A.

☑ No: Please check all that apply: √ Partial Waiver ___ Deferred √ Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

☐ Products in this class for this indication have been studied/labeled for pediatric population

☐ Disease/condition does not exist in children

☐ Too few children with disease to study

☐ There are safety concerns

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min____ kg____ mo.____ yr._0_ Tanner Stage____
Max____ kg____ mo.____ yr._12_ Tanner Stage____

Reason(s) for partial waiver:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**
- ☑ **Other: The fixed-dose combination at the proposed dosage is not suitable for children younger than 12 years of aged.**

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min____ kg____ mo.____ yr.____ Tanner Stage____
Max____ kg____ mo.____ yr.____ Tanner Stage____

Reason(s) for deferral:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**

Other:_____

Date studies ~~are~~ due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min____ kg____ mo.____ yr._12_ Tanner Stage____
Max____ kg____ mo.____ yr._Adult_ Tanner Stage____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Anthony M. Zeccola, M.A.
Senior Regulatory Management Officer

cc: NDA 21-605
HFD-960/ Rosemary Addy or Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

(revised 2-28-2005)

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Anthony Zeccola
3/17/05 09:05:12 AM

Debarment Certification

Schering Corporation hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning [redacted] (*Name of clinical investigator*), who participated as a clinical investigator in the submitted study "E/ S of Sch 483 Compared to DL and PSE in the Treatment of Subjects with SAR (*Name of clinical study*), is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

- ☐ any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;
- ☐ any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;
- ☐ any proprietary interest in the product tested in the covered study held by the clinical investigator;
- ☒ any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
Heribert Staudinger, MD	Vice-President, Allergy/Respiratory Diseases/Clinical Immunology
FIRM/ORGANIZATION: Schering-Plough Research Institute	
SIGNATURE	DATE: 13-APR-04

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 4 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14-72
Rockville, MD 20857

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Efficacy & Safety of SCH 483 Compared to Desloratadine and Pseudoephedrine in the Treatment of Subjects with Seasonal Allergic Rhinitis

Dr. [redacted] disclosed that he has/will receive payments from Schering-Plough in excess of $25,000 from honoraria and /or consultation. From the period of February 1, 2000 to February 1, 2001, Dr. [redacted] has a consultant's agreement in the amount of $100,000.

Comment:

This study was a randomized, multicenter, double blind, double dummy, parallel group study in [redacted] domestic sites. The study was designed to minimize any bias by an individual investigator or subject. Subjects were randomized and treated prior to breaking the blind.

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Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning _____ (*Name of clinical investigator*), who participated as a clinical investigator in the submitted study "E/ S of Sch 483 Compared to DL and PSE in the Treatment of Subjects with SAR" (*Name of clinical study*), is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

☐ any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

☐ any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;

☐ any proprietary interest in the product tested in the covered study held by the clinical investigator;

☒ any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
Heribert Staudinger, MD	Vice-President, Allergy/Respiratory Diseases/Clinical Immunology
FIRM/ORGANIZATION: Schering-Plough Research Institute	
SIGNATURE: HL/h	DATE: 13-APR-04

Paperwork Reduction Act Statement

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FORM FDA 3455 (7/01)

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DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Efficacy & Safety of SCH 483 Compared to Desloratadine and Pseudoephedrine in the Treatment of Subjects with Seasonal Allergic Rhinitis

Dr. [redacted] disclosed that she, her spouse and dependent children hold an equity of interest in Schering Plough stock in the amount of approximately $403,500.

Comment:

This study was a randomized, multicenter, double blind, double dummy, parallel group study in [redacted] domestic sites. The study was designed to minimize any bias by an individual investigator or subject. Subjects were randomized and treated prior to breaking the blind.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning _____ (*Name of clinical investigator*), who participated as a clinical investigator in the submitted study "E/ S of Sch 483 Compared to DL and PSE in the Treatment of Subjects with SAR" (*Name of clinical study*), is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

☐ any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

☐ any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;

☐ any proprietary interest in the product tested in the covered study held by the clinical investigator;

☒ any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
Heribert Staudinger, MD	Vice-President, Allergy/Respiratory Diseases/Clinical Immunology
FIRM/ORGANIZATION: Schering-Plough Research Institute	
SIGNATURE	DATE
	13-APR-04

Paperwork Reduction Act Statement

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FORM FDA 3455 (7/01)

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Efficacy & Safety of SCH 483 Compared to Desloratadine and Pseudoephedrine in the Treatment of Subjects with Seasonal Allergic Rhinitis

Dr. [redacted] disclosed that he, his spouse and dependent children hold an equity of interest in Schering Plough stock, 2000 shares.

Comment:

This study was a randomized, multicenter, double blind, double dummy, parallel group study in [redacted] domestic sites. The study was designed to minimize any bias by an individual investigator or subject. Subjects were randomized and treated prior to breaking the blind.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning [redacted], who participated as a clinical investigator in the submitted study "E/ S of Sch 483 Compared to DL and PSE in the Treatment of Subjects with SAR, is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Name of clinical investigator

Name of clinical study

Please mark the applicable checkboxes.

☐ any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

☐ any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;

☐ any proprietary interest in the product tested in the covered study held by the clinical investigator;

☒ any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
Heribert Staudinger, MD	Vice-President, Allergy/Respiratory Diseases/Clinical Immunology
FIRM/ORGANIZATION: Schering-Plough Research Institute	
SIGNATURE: [signature]	DATE: 13-APR-04

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 4 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to:

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Food and Drug Administration
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FORM FDA 3455 (7/01)

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DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

[redacted]

Efficacy & Safety of SCH 483 Compared to Desloratadine and Pseudoephedrine in the Treatment of Subjects with Seasonal Allergic Rhinitis

Dr. [redacted] disclosed that he, his spouse and dependent children hold an equity of interest in Schering Plough stock in IRAs and Pension plan in the approximate amount of $136,000.

Comment:

This study was a randomized, multicenter, double-blind, double dummy, parallel group study in [redacted] domestic sites. The study was designed to minimize any bias by an individual investigator or subject. Subjects were randomized and treated prior to breaking the blind.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning _____ (*Name of clinical investigator*), who participated as a clinical investigator in the submitted study "E/ S of Sch 483 Compared to DL and PSE in the Treatment of Subjects with SAR" (*Name of clinical study*), is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

☐ any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

☐ any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;

☐ any proprietary interest in the product tested in the covered study held by the clinical investigator;

☒ any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
Heribert Staudinger, MD	Vice-President, Allergy/Respiratory Diseases/Clinical Immunology
FIRM/ORGANIZATION: Schering-Plough Research Institute	
SIGNATURE	DATE: 8-APR-04

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 4 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to:

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Food and Drug Administration
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FORM FDA 3455 (7/01)

SLIN DOC APR 13 2004

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Efficacy & Safety of SCH 483 Compared to Desloratadine and Pseudoephedrine in the Treatment of Subjects with Seasonal Allergic Rhinitis

Dr. [redacted] disclosed that he, his spouse and dependent children hold an equity of interest in Schering Plough stock in the amount of approximately $100,000.

Comment:

This study was a randomized, multicenter, double blind, double dummy, parallel group study in [redacted] domestic sites. The study was designed to minimize any bias by an individual investigator or subject. Subjects were randomized and treated prior to breaking the blind.

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Public Health Service
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Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning [redacted] (*Name of clinical investigator*), who participated as a clinical investigator in the submitted study "E/ S of Sch 483 Compared to DL and PSE in the Treatment of Subjects with SAR" (*Name of clinical study*), is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

- ☐ any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;
- ☐ any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;
- ☐ any proprietary interest in the product tested in the covered study held by the clinical investigator;
- ☒ any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
Heribert Staudinger, MD	Vice-President, Allergy/Respiratory Diseases/Clinical Immunology
FIRM/ORGANIZATION: Schering-Plough Research Institute	
SIGNATURE: HSL	DATE: 13-APR-04

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 4 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to:

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DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Efficacy & Safety of SCH 483 Compared to Desloratadine and Pseudoephedrine in the Treatment of Subjects with Seasonal Allergic Rhinitis

Dr. — disclosed that he received payments from Schering-Plough in excess of $25,000 from honoraria and /or consultation. Since 1990, Dr. — has receved approximately $200,000 in honoraria and consultants fees.

Comment:

This study was a randomized, multicenter, double blind, double dummy, parallel group study in — domestic sites. The study was designed to minimize any bias by an individual investigator or subject. Subjects were randomized and treated prior to breaking the blind.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning [redacted], who participated as a clinical investigator in the submitted study "E/ S of Sch 483 Compared to DL and PSE in the Treatment of Subjects with SAR", is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Name of clinical investigator

Name of clinical study

Please mark the applicable checkboxes.

☐ any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

☐ any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;

☐ any proprietary interest in the product tested in the covered study held by the clinical investigator;

☒ any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
Heribert Staudinger, MD	Vice-President, Allergy/Respiratory Diseases/Clinical Immunology
FIRM/ORGANIZATION: Schering-Plough Research Institute	
SIGNATURE	DATE: 13-APR-04

Paperwork Reduction Act Statement

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Department of Health and Human Services
Food and Drug Administration
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Rockville, MD 20857

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FORM FDA 3455 (7/01)

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DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

[redacted]

Efficacy & Safety of SCH 483 Compared to Desloratadine and Pseudoephedrine in the Treatment of Subjects with Seasonal Allergic Rhinitis

Dr. [redacted] disclosed that he, his spouse and dependent children hold an equity of interest in Schering Plough stock, 3337 shares.

Comment:

This study was a randomized, multicenter, double blind, double dummy, parallel group study in [redacted] domestic sites. The study was designed to minimize any bias by an individual investigator or subject. Subjects were randomized and treated prior to breaking the blind.

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On Original

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form Approved: OMB No. 0910-0396
Expiration Date: February 28, 2006.

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

☒ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	P01875	
	See Attached Listing (Pages 1 - 7)	

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Heribert Staudinger, MD	Vice-President, Clinical Research Allergy/Respiratory Diseases/Clinical Immunology
FIRM / ORGANIZATION Schering-Plough Research Institute	
SIGNATURE	DATE
	16-APR-04

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

FDA 356h

P01875 Investigator List

Site #	Principal Investigator	Address	Sub-Investigators with No Financial Interests
01	Robert Anolik, MD	Allergy & Asthma Specialists, PC 470 Sentry Parkway East, Ste 200 Blue Bell, PA 19422	
02	James W. Baker, MD	Allergy Associates Res. Ctr. 545 N. E. 47th Ave., #310 Portland, OR 97213	
03	George W. Bensch, MD	Bensch Research Associates 4632 Georgetown Place, Suite C Stockton, CA 95207	
04	William E.Berger, MD	Southern California Research Center 27800 Medical Center Rd., Suite 150 Mission Viejo, CA 92691	
05	Edwin A. Bronsky, MD	Intermountain Clinical Research 150 South 1000 East Salt Lake City, UT 84102	
06	B. Lauren Charous, MD	Milwaukee Medical Clinic-Advanced Healthcare, SC 3003 W. Good Hope Rd. Milwaukee, WI 53209	

P01875 Investigator List

Site #	Principal Investigator	Address	Sub-Investigators with No Financial Interests
07	Lawrence D. Sher, MD	Peninsula Research Associates 501 Deep Valley Drive, Suite 201 Rolling Hills Estates, CA 90274	
08	Terry Denison, MD	HARI 5799 Broadmoor, Suite 138 Mission, KS 66202	
09	Donald J. Dvorin, MD	Allergic Disease Associates, P.C. 210 Ark R.d., Suite 109 Mt. Laurel, NJ 08054	
10	Mark H. Ellis, MD	CHOC/PSF Adult & Pediatric Allergy, Asthma, and Clinical Immunology 725 W. LaVeta #100 Orange, CA 92868	
11	Linda Ford, MD	The Asthma & Allergy Center, PC 401 E. Gold Coast Rd, Suite 326 Papillion, NE 68046	
12	Stanley Galant, MD	1201 W. La Veta, Ste 508 Orange, CA 92868	
13	Stanley Goldstein, MD	Island Medical Research, P.C. 242 Merrick Road Rockville Centre, NY 11570	
14	Gary N. Gross, MD	5499 Glenlake Dr., Ste 200 Dallas, TX 75231	
15	Robert E. Grubbe, MD	Center of Reseearch Excellence, LLC PO Box 7190	

P01875 Investigator List

Site #	Principal Investigator	Address	Sub-Investigators with No Financial Interests
		324 Monger Street Oxford, AL 36203	
16	Alan M. Heller, MD	San Jose Clinical Research, Inc. 2039 Forest Ave. Suite 203 San Jose, CA 95128	
17	Harold Kaiser, MD	Clinical Research Institute 825 Nicollet Mall, Suite 1633 Minneapolis, MN 55402	
18	Kenneth T. Kim, MD	Allergy Asthma & Respiratory Care Center, Inc. 2501 Cherry Ave., Suite 350 Long Beach, CA 90806	
19	Kathy L. Lampl, MD	Asthma & Allergy Associates 14808 Physicians Lane, Suite 211 Rockville, MD 20850	
20	Lawrence P. Landwehr, MD	Clinical Research of the Ozarks, Inc. 407A East Russell Ave., Suite 3 Warrensburg, MO 64093	
21	Daniel R. Rowe, MD	Palm Beach Research Center 1897 Palm Beach Lakes Boulevard, Suite 120 West Palm Beach, FL 33409	
22	Allen Lieberman, MD	HealthQuest Research, Ltd. 3807 Spicewood Springs Rd., Ste 250 Austin, TX 78759-8950	

P01875 Investigator List

Site #	Principal Investigator	Address	Sub-Investigators with No Financial Interests
23	Mark D. Livezey, M.D., Ph.D.	Allergy & Asthma Consultants, P.C. 5555 Peachtree - Dunwoody Road, Suite 325 Atlanta, GA 30342	
24	Clement A. Maccia, MD	65 Mountain Blvd. Extension, Ste 107 Warren, NJ 07059	
25	Anthony J. Weido, MD	Allergy and Asthma Associates 7505 Fannin Suite 515 Houston, TX 77054	
26	S. David Miller, M.D.	New England Clinical Studies 49 State Road, Watuppa Bldg., N. Dartmouth, MA 02747	
27	Dennis K. Ledford, MD	USF Asthma & Allergy Research Unit 13801 Bruce B. Downs Blvd, Suite 505 Tampa, FL 33613	
28	Robert Nathan, MD	Asthma & Allergy Associates, PC 2709 N. Tejon Street Colorado Springs, CO 80907	
29	Anjuli S. Nayak, MD	ICSL Clinical Studies	

P01875 Investigator List

Site #	Principal Investigator	Address	Sub-Investigators with No Financial Interests
		204 N. Prospect Road Bloomington, IL 61704	
30	Harold S. Nelson, MD	National Jewish Medical & Res. Div. Ctr 1400 Jackson St., Rm. A02 Denver, CO 80206	
31	Gary Lotner, M.D.	Rx Research 2171 Northlake Parkway, Suite 114 Tucker, GA 30084	
32	Patrick V. Perin, MD	185 Cedar Lane, Suite L-2 Teaneck, NJ 07666	
33	Warren W. Pleskow, MD	Radiant Research 317 N. El Camino Real, #506 Encinitas, CA 92024	
34	Paul H. Ratner, MD	Sylvana Research 7711 Louis Pasteur Dr., Suite 406 San Antonio, TX 78229	
35	Amar Bukhari, MD	Asthma & Allergy Clinical Research. 254 Easton Ave., CARES Bldg. 4th Fl. New Brunswick, NJ 08903-0591	
36	Nathan Segall, MD	Clinical Research Atlanta 980 Johnson Ferry Road, Suite 1080 Atlanta, GA 30342	
37	Guy A. Settipane, MD	Asthma, Nasal Disease & Allergy	

P01875 Investigator List

Site #	Principal Investigator	Address	Sub-Investigators with No Financial Interests
		Research Center of New England 95 Pitman St. Providence, RI 02906	
38	Ellen R. Sher, MD	Atlantic Allergy, Asthma & Immun. 802 West Park Ave., Suite 213 Ocean, NJ 07712	
39	Leonard J. Caputo, MD	The Asthma and Allergy Institute 124 University Blvd., Suite 2 Mobile, AL 36608	
40	Michael C. Young, MD	South Shore Allergy & Asthma Specialists, P.C. 851 Main St., Suite 21 S. Weymouth, MA 02190	
41	Martha M. Tarpay, MD	Allergy, Asthma & Clinical Research. Center 4200 W. Memorial Rd., Suite 206 Oklahoma City, OK 73120	
42	Robert G. Townley, MD	Creighton University Center. for Allergy, Asthma & Immunology 2500 California Plaza Omaha, NE 68178	
43	Julius H. Van Bavel, MD	Allergy & Asthma Associates	

P01875 Investigator List

Site #	Principal Investigator	Address	Sub-Investigators with No Financial Interests
		3410 Far West Blvd., Suite 146 Austin, TX 78731	
44	Steven G. Weiss, MD	Florida, Allergy, Asthma and Immunology 3251 McMullen Booth Rd. Clearwater, FL 33761	
45	Martha White, MD	Institute for Asthma & Allergy, PC 5454 West Wisconsin Avenue, Ste 1700 Chevy Chase, MD 20815	
46	John A. Winder, MD	Toledo Center for Clinical Research. 5860 Alexis Road., Suite B Sylvania, OH 43560	
47	Richard A. Wyatt, MD	Asthma & Allergy Res. Ctr. Institute for Research & Education 3800 Nicollet Blvd. Minneapolis, MN 55416	
48	Emil Burger, Jr., MD	National Clinic Research Institute 8301 E. Florence Ave, Suite 104-103 Downey, CA 90621	

SCHERING-PLOUGH RESEARCH INSTITUTE

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form Approved: OMB No. 0910-0396
Expiration Date: February 28, 2006.

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

☒ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	P01884	
	See Attached Listing (Pages 1 - 7)	

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Heribert Staudinger, MD	Vice-President, Clinical Research Allergy/Respiratory Diseases/Clinical Immunology
FIRM / ORGANIZATION Schering-Plough Research Institute	
SIGNATURE	DATE
	16 AUG 04

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

P01884 Investigator List

Site #	Principal Investigator	Address	Sub Investigators with No Financial Interests
01	Charles Banov, MD	Radiant Research, Charleston - North 9165 University Blvd Charleston, SC 29406	
02	Robert B. Berkowitz, MD	Rx Research 335 Parkway 575, Suite 110 Woodstock, GA 30188	
03	David I. Bernstein, MD	Bernstein Clinical Research, LLC 8444 Winton Road Cincinnati, OH 45231	
04	Mark Boguniewicz, MD	National Jewish Med. & Res. Ctr. K309 C Resp. Res. Dept. (809 Reg) 1400 Jackson St. Denver, CO 80206	
05	Stuart Rhein, MD	ClinCare - MetroWest 212 Carnegie Row Norwood, MA 02062 (Dr's Direct office) 475 Franklin Street, Suite #206 Framingham, MA 01701	
06	Paul Chervinsky, MD	New England Clinical Studies 49 State Rd., Watuppa Bldg. No. Dartmouth, MA 02747	
07	John J. Condemi, MD	AAIR Research Center 919 Westfall Rd., Bldg. B Rochester, NY 14618	

P01884 Investigator List

Site #	Principal Investigator	Address	Sub Investigators with No Financial Interests
08	Jonathan Corren, MD	Allergy Medical Clinical 11620 Wilshire Blvd., #200 Los Angeles, CA 90025	
09	James Stubbert, MD	ClinCare - Fall River Durfee Union Mills, 187 Plymouth Avenue, Bldg.8 Fl. 2 Fall River, MA 02722	
10	Bruce F. Friedman, MD	Allergy & Asthma Associates 11180 Warner Ave., Suite 255 Fountain Valley, CA 92708	
11	Pinkus Goldberg, MD	Clinical Research Center of Indiana 3266 N. Meridian, #702 Indianapolis, IN 46208	
12	David Gossage, MD	Allergy, Asthma & Sinus Center 801 Weisgarber Rd., #200 Knoxville, TN 37909	
13	Gregory Gottschlich, MD	New Horizons Clinical Research 10475 Reading Rd., Suite 308 Cincinnati, OH 45241	

P01884 Investigator List

Site #	Principal Investigator	Address	Sub Investigators with No Financial Interests
14	Frank C. Hampel, Jr., MD	Central Texas Health Research 705-A Landa Street New Braunfels, TX 78130	
15	Nancy G. Campbell, M.D.	Breco Research 902 Frostwood St., Ste 223 Houston, TX 77024	
16	Robert Jacobs, MD	Biogenics Research Institute 8279 Fredericksburg Road San Antonio, TX 78229	
17	Nicholas A. Nayak, MD	ICSL – Clinical Studies 214 NE Glen Oak Ave., Ste 605 Peoria, IL 61603-4300	
18	Edward M. Kerwin, MD	**Clinical Research. Institute of Southern** 3860 Crater Lake Ave, Suite B Medford, OR 97504	
19	Craig F. LaForce, MD	North Carolina Clinical Research 4301 Lake Boone Trail, Suite 309A Raleigh, NC 27607	
20	Michael Lawrence, MD	Center for Clinical Research 35 Summer Street, Suite 202B Taunton, MA 02780	
21	Jeffrey G. Leflein, MD	Respiratory Medicine Research Institute of Michigan,P.L.C. 5333 McAuley Drive, Ste R1018 Ypsilanti, MI 48197	
22	Donald S. Levy, MD	705 W. La Veta, Suite 101 Orange, CA 92868-4447	
23	W. R. Lumry, MD	9900 N. Central Espwy, Suite 525 Dallas, TX 75231	

SCHERING-PLOUGH RESEARCH INSTITUTE

P01884 Investigator List

Site #	Principal Investigator	Address	Sub Investigators with No Financial Interests
24	David B.K. Golden, MD	Atlantic Asthma & Allergy Ctr., Inc. 7939 Honeygo Blvd., Suite 219 Baltimore, MD 21236	
25	Rogelio Menendez, MD	Allergy & Asthma Research Center of El Paso, PA 10470 Vista Del Sol, Suites 100 & 203 El Paso, TX 79925	
26	Kevin Murphy, MD	Midwest Asthma & Allergy Clinic 8552 Cass Street Omaha, NE 68114	
27	John J. Murray, MD	Vanderbilt University Medical Ctr. Asthma Sinus Allergy Program 2611 West End Ave., #120 Nashville, TN 37203	
28	David S. Pearlman, MD	Clinical Research Ctrs. of Colorado, PC 1450 S. Havana St., Suite 620 Aurora, CO 80012	
29	Andrew Pedinoff, MD	Princeton Center for Clinical Research. 414 Executive Drive Princeton, NJ 08540	
30	Frank J. Picone, MD	The Clinical Res. Ctr. of Allergy & Asthma Consultants 709 Sycamore Avenue Tinton Falls, NJ 07701	

P01884 Investigator List

Site #	Principal Investigator	Address	Sub Investigators with No Financial Interests
31	Jacob Pinnas, MD	Arizona Clinical Studies 1601 N. Tucson Blvd., #32 Tucson, AZ 85716	
32	Stephen J. Pollard, MD	Allergy & Asthma Associates 1700 Bluegrass Avenue, Suite 400 Louisville, KY 40215	
33	Bruce M. Prenner, MD	Allergy Assoc. Medical Group, Inc. 6386 Alvarado Ct., Suite #210 San Diego, CA 92120	
34	Anthony Rooklin, MD	Allergy Research Associates 1 Medical Center Blvd. President's House Upland, PA 19013	
35	Richard Brodie, MD	ClinCare - Brookline 70 Parker Hill Avenue, Suite 500 Brookline, MA 02120	
36	Emilio F. A. Berberabe, Jr., MD	Center For Clinical Research 2810 West Charleston Blvd., Ste #H-83 Las Vegas,NV 89102	
37	Eric Schenkel, MD	Valley Clinical Research Center 3729 Easton-Nazareth Hwy., Ste 202 Easton, PA 18045	
38	Howard Schwartz, MD	University Hospitals of Cleveland 11100 Euclid Avenue Cleveland, OH 44106	

P01884 Investigator List

Site #	Principal Investigator	Address	Sub Investigators with No Financial Interests
39	Allen T. Segal, MD	Allergy Associates Research 13601 Preston Rd., Suite 310E Dallas, TX 75240	
40	Tommy C. Sim, MD	Family Center. for Asthma & Allergic Diseases 357 E. Parkwood Drive (FM 528) Friendswood, TX 77546	
41	G. Edward Stewart II, MD	2100 SE 17th St., Suite 701 Ocala, FL 34471	
42	William N. Sokol, MD	Health Research Institute 2011 Westcliff Dr., Suite #7 Newport Beach, CA 92660	
43	Jonathan Tarro, MD	ClinCare Johnston 1524 Atwood Avenue Johnston, RI 02919	
44	Mark L. Vandewalker, M.D	Allergy & Asthma Consultants 1191 Highway KK, Suite 201 Osage Beach, MO 65065	
46	Steven Weinstein, MD	Allergy & Asthma Specialists Medical Group 17742 Beach Blvd., Suite 310 & 340 Huntington Beach, CA 92647	
47	James D. Wolfe, MD	Allergy & Asthma Associates of Santa Clara Valley Res. Ctr. 4155 Moorpark Ave., Suite 6 San Jose, CA 95117	
48	Karl V. Sitz, MD	Little Rock Allergy & Asthma Clinic, P.A. 18 Corporate Hill Drive, Suite 110 Little Rock, AR 72205	

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P01884 Investigator List

Site #	Principal Investigator	Address	Sub Investigators with No Financial Interests
49	Anjuli S. Nayak, MD	ICSL-Clinical Studies 204 N. Prospect Road Bloomington, IL 61704	[redacted]

SCHERING CORPORATION

2000 GALLOPING HILL ROAD KENILWORTH, N.J. 07033
TELEPHONE: (908) 298-4000

February 10, 2005

Badrul A. Chowdhury, M.D., PhD, Director
Division of Pulmonary and Allergy Drug Products, HFD-570
FDA - Center for Drug Evaluation and Research
Office of Drug Evaluation II
Document Control Room 8B45
5600 Fishers Lane
Rockville, MD 20857

NDA 21-605
CLARINEX-D® 24 HOUR Tablet
(desloratadine 5mg/ pseudoephedrine sulfate 240mg)

SUBJECT: AMENDMENT NEW DRUG APPLICATION

Dear Dr. Chowdhury:

Please find attached an amendment to the New Drug Application (NDA) (pursuant to 21 CFR Part 314) for the use of CLARINEX-D® 24 HOUR Extended Release Tablets (desloratadine 5mg/ pseudoephedrine sulfate 240 mg) for the relief of symptoms of allergic rhinitis, including nasal congestion, in adults and children 12 years of age and older.

As the NDA references publicly available information in the published Final Monograph for OTC Nasal Decongestant Products (21 CFR 341) for pseudoephedrine sulfate, we are updating the 356h application form at the Agency's request from an application under Section 505(b)1, as stipulated in the original NDA submission, to an application under Section 505(b)2. A revised form 356h is attached.

We are also amending section 14 of this NDA to include a patent certification (**Attachment 1**) pursuant to 21 CFR § 314.50(i)(1)(Ii) certifying that there are no relevant patents. This certification is being made in accordance with the provisions of 21 CFR § 314.50(i)(1)(ii) implementing Section 505(b)(2) because the aforementioned NDA does not rely on investigations or other data of any listed drug for which we do not have a right of reference (see **Attachment 2**).

As set forth in the NDA, clinical safety and efficacy of the desloratadine/pseudoephedrine product is demonstrated by the two clinical studies contained within the CLARINEX-D® 24 Hour Tablets NDA. Our own

loratadine/pseudoephedrine NDAs [CLARITIN-D 24 (NDA 20-470) and CLARITIN-D 12 (NDA 19-670)] are being relied on for certain data related to the pseudoephedrine extended release tablet core. Consequently, we are only relying on the Final Monograph for OTC Nasal Decongestant Products (21 C.F.R. 341) for the limited purposes of referencing the publicly available pre-clinical pseudoephedrine data set forth in that published Final Monograph.

As discussed with Mr. Tony Zeccola on January 27, 2005, we understand that this submission simply updates/corrects the administrative file and will have no impact on the review clock.

Should you have any questions please call Ms. Diane deBruin at (908) 740-4306 or Mr. David De Sousa at (908) 740-4285, and for chemistry related questions please call Mr. Satish Joshi at (908) 740-4355.

Please be advised that the material and data contained in this submission are considered to be confidential. The legal protection of such confidential commercial material is claimed under the applicable provisions of 18 U.S.C., Section 1905 or 21 U.S.C., Section 331(j) as well as the FDA regulations.

Sincerely,

Diane deBruin
Senior Manager & Liaison
Global Regulatory Affairs

DD:cv

Attachments

Appears This Way
On Original

ATTACHMENT 1

Pursuant to the requirements of 21 CFR § 314.50(i)(1)(ii), we are hereby submitting the following patent statement for Schering Corporation's CLARINEX-D® 24 Hour Tablet NDA No. 21-605. An explanation of the basis for this statement is set forth in **Attachment 2** of this submission.

In the opinion and to the best knowledge of Schering Corporation, there are no patents that claim the drug or drugs on which investigations that are relied upon in this application were conducted or that claim a use of such drug or drugs.

2/10/05

Henry Hadad
Staff Vice President-Patent Law

Appears This Way
On Original

ATTACHMENT 2

Consistent with the provisions of 21 C.F.R. § 314.50(i)(1)(ii), the NDA submission for CLARINEX -D® 24 Hour Tablets does not rely on investigations or other data of any reference listed drug for which we do not have a right of reference. Therefore, as set forth in that regulatory provision, there are no relevant patents that claim the drug or drugs on which investigations that are relied upon in this application were conducted or that claim a use of such drug or drugs. Schering Corporation's determination in this regard is based on the following:

1. CLARINEX -D® 24 Hour Tablet NDA does not refer to investigations or other data provided by a Reference Listed Drug (RLD) for which we do not have a right of reference.

2. The CLARINEX -D® 24 Hour Tablet NDA contains data to support the clinical safety and efficacy of the combination desloratadine/pseudoephedrine product. Schering Corporation is the owner of data for desloratadine and makes reference to the CLARINEX NDA (21-165).

3. As discussed with the Division of Pulmonary and Allergy Products (DPADP) prior to submission of the CLARINEX-D® 24 Hour Tablets NDA 21-605, the pseudoephedrine comparator to which the combination was compared in the clinical program was the pseudoephedrine extended release core utilized in both the CLARINEX-D® 24 and the CLARITIN-D 24 products. This pseudoephedrine extended release core was developed and is owned by Schering Corporation.

4. In the clinical pharmacokinetic program, pseudoephedrine from the CLARINEX-D® 24 hour combination was found to be bioequivalent to that following administration of the pseudoephedrine from the extended release core. As the pharmacokinetic profile of pseudoephedrine was established following administration of both CLARINEX -D® 24 and the pseudoephedrine extended release core, the CLARINEX -D® 24 Hour Tablets NDA 21-605 refers to data contained within the CLARITIN-D 24 NDA (20-470) and CLARITIN-D 12 NDA (19-670) (e.g. see Section 5.B Toxicology Technical Summary, Section 8.J. Integrated Summary of Benefits and Risk). Schering Corporation owns all of the data in these NDAs.

5. The two clinical safety and efficacy studies provided in the CLARINEX-D® 24 Hour Tablets NDA demonstrate the clinical superiority of the combination desloratadine/pseudoephedrine product (CLARINEX-D® 24) to that of the

individual components (i.e. desloratadine 5 mg tablet and pseudoephedrine 240 mg extended release core). Schering Corporation is the owner of these clinical data.

6. To further support the safety of pseudoephedrine sulfate, reference is also made to the information set forth in the published Final Monographs for OTC Nasal Decongestant Products (21 CFR 341) for the limited purposes of referencing the publicly available pre-clinical data therein supporting the safety of pseudoephedrine.

7. In an application such as this one, a patent certification of "no relevant patents" pursuant to 21 CFR § 314.50(i)(1)(ii) is appropriate. The plain language of the regulations and the statutory provisions they implement reflect that patent certifications to patents listed in the Orange Book for an approved reference listed drug (RLD) are only necessary if a 505(b)(2) application is relying on the Agency's prior finding of safety and efficacy with respect to an RLD and thus the investigations or data submitted in support of that approved RLD.

This view is consistent with FDA's position in *King Pharmaceuticals v. FDA* (Civ. No. 01058) as presented in proceedings before the United States District Court for the District of Columbia. *See*, FDA's Memorandum in Opposition to Plaintiff's Motion for a Temporary Restraining Order and a Preliminary Injunction dated July 1, 2004. In its brief, FDA begins by quoting the statutory requirements for patent certification as they apply to 505(b)(2) applications:

> (2) An application submitted under *paragraph (1) for a drug for which the investigations described in clause (A) of such paragraph and relied upon by the applicant for approval of the application* were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted shall also include—
>
> (A) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the drug *for which such investigations were conducted* or which claims a use for such drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under paragraph (1) or subsection (c) of this section....

21 U.S.C. § 355(b)(2) (emphasis added).

The Agency's brief then goes on to present the following analysis of this statutory provision:

> Section 355(b)(2)'s reference to clause (A) in the phrase "for a drug for which the investigations described in clause (A) of such paragraph" refers to § 355(b)(1)(A). Section 355(b)(1)(A) states that NDAs must contain "(A) *full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use....*" (emphasis added). The next phrase in § 355(b)(2) - *"and relied upon by the applicant for approval of the application"* – means that the applicant is relying on findings of safety and efficacy that were made for another drug to fill in gaps and obtain approval of its own application. The certification requirement in § 355(b)(2)(A) applies only to patents that claim such other drugs for which such safety and effectiveness studies were conducted and when the current application relies upon those studies.
>
> FDA's implementing regulations are fully consistent with this interpretation. 21 C.F.R. § 314.50(i)(1)(i) provide that a § 355(b)(2) application is required to contain "a certification with respect to each patent...that...claims a drug...*on which investigations that are relied upon by the applicant for its approval* of its application were conducted or that claims an approved use for such drug and for which information is required to be filed under section 355(b) and (c) of the [FDCA] and 314.53." (emphasis added). See also 21 C.F.R. § 314.3(b) definition of § 355(b)(2) application) and § 314.54(a)(1)(vi).

Memorandum in Opposition to Plaintiff's Motion for a Temporary Restraining Order and a Preliminary Injunction, pages 15-16.

Since Schering's NDA submission for CLARINEX-D® 24 Hour Tablets does not rely on data of any reference listed drug for which we do not have a right of reference, a certification of "no relevant patents" is appropriate under the applicable regulations and the statutory provisions they implement.

Appears This Way
On Original

Memorandum of Teleconference

Date: February 2, 2005

Time: 11:30 AM

Location: 10B45 Conference Room

Application: N21-605 Clarinex-D24 (desloratadine/pseudophederine) Tablets

Representatives of Division of Pulmonary and Allergy Drug Products

Badrul A. Chowdhury, M.D., Ph.D., Division Director
Richard Lostritto, Ph.D., CMC Team Leader
Prasad Peri, Ph.D., CMC Reviewer
Peter Starke, M.D., Clinical Team Leader
Anthony Zeccola, Regulatory Management Officer

Representatives of Schering

Nicholas Pelliccione Ph.D., Vice President CMC, Global Regulatory Affairs
Satish Joshi, Senior Manager, CMC Global Regulatory Affairs
David De Sousa, Senior Director, Global Regulatory Affairs
Diane Debruin, Senior Manager Global Regulatory Affairs
Jack Rosen Ph.D., Director, Analytical Development
Stephen Liebowitz, Ph. D., Director, Pharmaceutical Development
Richard Lorber, M.D., Senior Director, Clinical Research

Background: This teleconference was held in response to discuss the expiry for NDA 21-605, Clarinex-D24 (desloratadine/pseudophederine) Tablets.

Discussion: Dr. Peri opened the discussion with the following comments:

"Based on the data submitted in the NDA and the lack of stability of the drug product at temperatures above 25°C, only the following storage statement supports the proposed 24 month expiry dating period. Store at 25C (77F). Caution: Heat sensitive; do not store above 25°C (77°F)".

Because the role of % relative humidity is apparent but not yet quantified for this drug product's stability problems, any 2-8°C storage for to-be-marketed consideration must be supported by full-term data."

Schering indicated that they will take this information into consideration and will respond following internal discussion. They also indicated that given the time frame for the PDUFA action date, if they

disagree with our suggested expiry, they will provide that information post approval via a CMC supplement.

Addendum to Teleconference Minutes:

At the end of the discussion Dr. Lostritto indicated that we would be sending addition CMC comments that pertain to the drug products (see below).

a. Provide particle size data from commercial lots of hypromellose used for the manufacture of claritin D24. Clearly indicate with appropriate data, if the proposed acceptance criteria for the particle size of hypromellose can adequately control the release rate of pseudoephedrine sulfate.

b. Update the NDA with UV and IR spectra of samples of Blue lake blend.

c. Provide suitable justification for the selection of a sub coat and finish coat .

d. Update the NDA to specify clearly how many tablets (number of tablets sampled for each test, and if a mean tablet weight is used) are sampled from a given batch during in-process testing.

f. Revise the acceptance criteria for all impurities to .

g. Revise the acceptance criterion for desloratadine release rate to Q= in 30 minutes.

Discussion

Biopharm Comments

Please provide 3-OH desloratadine to desloratadine ratios at 12 hours for all pediatric subjects included in the PK and safety studies (P02798 and P03016).

The original protocol stated that a total of 8 children (2 for each age group) would be included in the 2 to 5 age group in study P02798, but only 4 were enrolled. Please provide an explanation of this discrepancy.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Anthony Zeccola
2/3/05 03:36:20 PM
CSO

Memorandum of Telephone Facsimile Correspondence

Date: 9/30/2004

To: Carlos Langezaal
Senior Manager, Drug Regulatory Affairs

From: Anthony Zeccola
Regulatory Management Officer
Division of Pulmonary Drug Products
FDA

Subject: Request for Information – NDA 21-605

Total Pages: 2

We are providing the attached information via telephone facsimile for your convenience, to expedite the progress of your drug development program. This material should be viewed as unofficial correspondence. Please feel free to contact me if you have any questions regarding the contents of this transmission.

Thank you.

{See appended electronic signature page}

Anthony M. Zeccola
Regulatory Management Officer
Division of Pulmonary Drug Products

Please provide the following information to assist in our review of NDA 21-605:

Submit the following information either as part of the regular 120 Day Safety Update or as a separate submission , whichever can be accomplished sooner:

1. A review of worldwide postmarketing adverse event reports for single ingredients desloratadine and pseudoephedrine. Include a summary, narrative analysis, and discussion of frequent adverse eventss and adverse eventss of special concern, including cardiac, hepatic, renal, neurologic (somnolence, seizure), and genitourinary (hypospadias) events. Cover the period of time since December 21, 2001, the date of the approval of Clarinex Tablets, 5 mg (NDA 21-165) until the cut-off date for the required safety update.

2. A review of the worldwide medical literature for articles relevant to the safety of single ingredients desloratadine and pseudoephedrine. Include a list of references identified by your search, copies of relevant articles, and a discussion of the relevant articles. Cover the period of time since December 21, 2001, the date of the approval of Clarinex Tablets, 5 mg (NDA 21-165) until the cut-off date for the required safety update.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Anthony Zeccola
9/30/04 02:46:01 PM
CSO

Memorandum of Telephone Facsimile Correspondence

Date: May 20, 2004

To: Carlos Langezaal

From: Anthony Zeccola

Subject: Request for Information – NDA 21-605

Total Pages: 3 (Including cover and electronic signature pages)

We are providing the attached information via telephone facsimile for your convenience, to expedite the progress of your drug development program. This material should be viewed as unofficial correspondence. Please feel free to contact me if you have any questions regarding the contents of this transmission.

Thank you.

{See appended electronic signature page}

Anthony M. Zeccola
Regulatory Management Officer
Division of Pulmonary Drug Products

Please provide the following information to assist in our review of NDA 21-605:

Reference is made to your desloratadine new drug application (NDA 21-165) and a submission dated November 13, 2003, in the NDA. The submission contains a study report entitled "24-month oral carcinogenicity study of SCH 34117 (desloratadine) in mice" (SN 97255).

We are currently reviewing the study and have found the study report inadequate for review. Specifically, the report did not contain tumor-finding data in a computer-readable format as described in the following two guidance documents: 1) Regulatory Submission in Electronic Format; General Considerations; and 2) Regulatory Submission in Electronic Format; New Drug Applications. These documents were issued in January 1999 and are available online at http://www.fda.gov/cder/guidance.

To facilitate the regulatory review, please submit the electronic data as described in the above guidance. The data must include the tumor-finding data files named TUMOR.XPT.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Anthony Zeccola
5/20/04 04:22:29 PM
CSO

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information		
NDA 21-605	Efficacy Supplement Type SE-	Supplement Number
Drug: Clarinex D 24 Hour		Applicant: Schering Corporation
RPM: Zeccola		HFD-570 Phone # 301-827-1058

Application Type: ( ) 505(b)(1) (X) 505(b)(2) (This can be determined by consulting page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.) **If this is a 505(b)(2) application, please review and confirm the information previously provided in Appendix B to the NDA Regulatory Filing Review. Please update any information (including patent certification information) that is no longer correct.** ( ) Confirmed and/or corrected	Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)): pseudoephederine sulfate (Final Monograph for OTC Nasal Decongestant Products)

❖ Application Classifications:	
• Review priority	(X) Standard ( ) Priority
• Chem class (NDAs only)	3
• Other (e.g., orphan, OTC)	
❖ User Fee Goal Dates	March 3, 2005
❖ Special programs (indicate all that apply)	(X) None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review ( ) CMA Pilot 1 ( ) CMA Pilot 2
❖ User Fee Information	
• User Fee	(X) Paid UF ID number 4477
• User Fee waiver	( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other (specify)
• User Fee exception	( ) Orphan designation ( ) No-fee 505(b)(2) (see NDA Regulatory Filing Review for instructions) ( ) Other (specify)
Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes (X) No

• This application is on the AIP	( ) Yes (X) No
• Exception for review (Center Director's memo)	
• OC clearance for approval	
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification & certifications from foreign applicants are cosigned by US agent.	(X) Verified
❖ Patent	
• Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	( ) Verified
• Patent certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.	21 CFR 314.50(i)(1)(*i*)(A) ( ) Verified 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
• [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).	
• [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). *(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next box below (Exclusivity)).*	( ) N/A (no paragraph IV certification) ( ) Verified
• [505(b)(2) applications] For each paragraph IV certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation. Answer the following questions for each paragraph IV certification: (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification? (Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e))). *If "Yes," skip to question (4) below. If "No," continue with question (2).* (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)? *If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).* *If "No," continue with question (3).* (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?	( ) Yes ( ) No ( ) Yes ( ) No ( ) Yes ( ) No

(Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 ~~CFR~~ 314.107(f)(2))).	
If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.	
(4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?	( ) Yes ( ) No
If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).	
If "No," continue with question (5).	
(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification? (Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).	( ) Yes ( ) No
If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).	
If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.	
❖ Exclusivity (approvals only)	
• Exclusivity summary • Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)	NO
• Is there existing orphan drug exclusivity protection for the "same drug" for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.*	( ) Yes, Application #_____ (X) No
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	

General Information	
Actions	
• Proposed action	(X) AP ( ) TA ( ) AE ( ) NA
• Previous actions (specify type and date for each action taken)	
• Status of advertising (approvals only)	( ) Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	( ) Yes (X) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	(X) None ( ) Press Release ( ) Talk Paper ( ) Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable))	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	2/15/05
• Most recent applicant-proposed labeling	12/2/04
• Original applicant-proposed labeling	
• Labeling reviews (including DDMAC, DMETS, DSRCS) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	
• Applicant proposed	
• Reviews	
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	
• Documentation of discussions and/or agreements relating to post-marketing commitments	
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	
❖ Memoranda and Telecons	
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	
• Pre-NDA meeting (indicate date)	
• Pre-Approval Safety Conference (indicate date; approvals only)	
• Other	
❖ Advisory Committee Meeting	
• Date of Meeting	
• 48-hour alert	
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	

Summary/Application Review(s)	
Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	
Clinical Information	
❖ Clinical review(s) *(indicate date for each review)*	2/11/05
❖ Microbiology (efficacy) review(s) *(indicate date for each review)*	N/A
❖ Safety Update review(s) *(indicate date or location if incorporated in another review)*	Clinical Review
❖ Risk Management Plan review(s) *(indicate date/location if incorporated in another rev)*	N/A
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	
❖ Demographic Worksheet *(NME approvals only)*	
❖ Statistical review(s) *(indicate date for each review)*	
❖ Biopharmaceutical review(s) *(indicate date for each review)*	2/3/05
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	N/A
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	N/A
• Bioequivalence studies	N/A
CMC Information	
❖ CMC review(s) *(indicate date for each review)*	
❖ Environmental Assessment	
• Categorical Exclusion *(indicate review date)*	
• Review & FONSI *(indicate date of review)*	
• Review & Environmental Impact Statement *(indicate date of each review)*	
❖ Microbiology (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	N/A
❖ Facilities inspection (provide EER report)	Date completed: ( ) Acceptable ( ) Withhold recommendation
❖ Methods validation	( ) Completed ( ) Requested ( ) Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	2/16/05
❖ Nonclinical inspection review summary	
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	
❖ CAC/ECAC report	

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

PRESCRIPTION DRUG USER FEE COVER SHEET

Form Approved: OMB No. 0910-0297
Expiration Date: December 31, 2006.

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm

1. APPLICANT'S NAME AND ADDRESS
Schering Corporation
2000 Galloping Hill Road
Kenilworth, New Jersey 07033

ATTN: Dalena DeGrezia

2. TELEPHONE NUMBER *(Include Area Code)*
(908) 740-2545

3. PRODUCT NAME
CLARINEX-D 24 HOUR Extended Release Tablets

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER
NDA 21-605

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?
☒ YES ☐ NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW:

☒ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

_____
(APPLICATION NO. CONTAINING THE DATA).

6. USER FEE I.D. NUMBER
User Fee #4477

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92
(Self Explanatory)

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
(See item 7, reverse side before checking box.)

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act
(See item 7, reverse side before checking box.)

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY
(Self Explanatory)

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FORTHIS APPLICATION?
☐ YES ☒ NO
(See Item 8, reverse side if answered YES)

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

and

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Drive, Room 3046
Rockville, MD 20852

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Dalena DeGrezia	Dalena DeGrezia Global Regulatory Affairs Associate	4/16/2004

FORM FDA 3397 (12/03)

PSC Media Arts (301) 443-1090 EF