

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-993

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

**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

21-993

NAME OF APPLICANT / NDA HOLDER

Schering-Plough HealthCare Products

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)

Claritin ® RediTabs® 12 Hour Tablets

ACTIVE INGREDIENT(S)

loratadine

STRENGTH(S)

5 mg

DOSAGE FORM

orally disintegrating tablet

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 file 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

b. Issue Date of Patent

c. Expiration Date of Patent

d. Name of Patent Owner

Address (of Patent Owner)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

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)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

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

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? 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 Patent 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 approved 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.

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

Doreen Frank

02/10/2006

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

Doreen Frank
Director, Regulatory Affairs

Address

556 Morris Avenue

City/State

Summit, NJ

ZIP Code

07901-1330

Telephone Number

908-473-1655

FAX Number (if available)

908-473-1741

E-Mail Address (if available)

doreen.frank@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.

EXCLUSIVITY SUMMARY

NDA # 21-993

SUPPL #

HFD # 560

Trade Name Claritin RediTabs 12 Hour

Generic Name loratadine

Applicant Name Schering-Plough HealthCare Products

Approval Date, If Known

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES

NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES

NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

no

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 19-658

Claritin 10mg tablets

NDA# 20-704

Claritin 10mg ODT

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)

IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

- a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

- b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

Investigation #2

YES

Explain:

!
!

! NO

! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES

NO

If yes, explain:

Name of person completing form: Neel Patel

Title: Project Manager

Date: 10-11-2006

Name of Office/Division Director signing form: Andrea Leonard-Segal

Title: Division Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

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

/s/

Andrea Segal
12/12/2006 03:58:05 PM

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA #: 21-993 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: February 13, 2006 PDUFA Goal Date: December 13, 2006

HFD 560 Trade and generic names/dosage form: Claritin RediTabs 12 Hour (5 mg loratadine) orally disintegrating tablets

Applicant: Schering-Plough HealthCare Products Therapeutic Class: antihistamine

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 current application under review must have pediatric studies: *Completed, Deferred, and/or Waived.*

Number of indications for this application(s): 1

Indication #1: relief of symptoms of hay fever or other respiratory allergies

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
 Other: _____

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 (fill in applicable criteria below):

Min ____ kg ____ mo. 0 yr. ____ Tanner Stage ____
Max ____ kg ____ mo. 6 yr. ____ Tanner Stage ____

Reason(s) for partial waiver:

See the checked box below and Section D. Allergic rhinitis is rare in infants < 6 months

- 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: _____

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 (fill in applicable criteria below):

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 (fill in applicable criteria below):

Min ____ kg ____ mo. 6 yr. ____ Tanner Stage ____
Max ____ kg ____ mo. ____ yr. Adult Tanner Stage ____

Comments:

The sponsor has completed studies down to the age of 6 months under NDA 20-641, Children Claritin Syrup. We do not ask for studies under 6 months of age for allergic rhinitis because this condition is rare in this age group. We are giving the sponsor a partial waiver for infants < 6 months.

NDA 21-993

Page 3

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}

Regulatory Project Manager

**cc: NDA 21-993
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 6-23-2005)**

**APPEARS THIS WAY
ON ORIGINAL**

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

/s/

Neel Patel
12/12/2006 03:50:53 PM

Schering-Plough HealthCare Products 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.



John O'Mullane, Ph.D.
Group Vice President, Research and Development
Schering-Plough HealthCare Products, Inc.

13 OCT 2006

Date

**CERTIFICATION: FINANCIAL INTERESTS AND
ARRANGEMENTS OF CLINICAL INVESTIGATORS**

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).

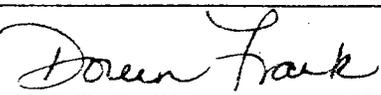
Please mark the applicable checkbox.

- (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	Protocol No. CL2005-02 Lawrence A. Galitz, M.D., Principal Investigator _____ Sub-investigator _____ Sub-investigator _____ Sub-investigator	SFBC International, Inc. 11190 Biscayne Boulevard Miami, Florida 33181-3405 SFBC International, Inc. (screening only) 2060 N.W. 22 nd Avenue Miami, FL 33142
	Protocol No. CL2004-01 Lawrence A. Galitz, M.D., Principal Investigator _____ Sub-investigator _____ Sub-investigator _____ Sub-investigator _____ Sub-investigator	SFBC International, Inc. 11190 Biscayne Boulevard Miami, Florida 33181-3405

- (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 Doreen Frank	TITLE Director, Regulatory Affairs
FIRM / ORGANIZATION Schering Plough HealthCare Products, Inc.	
SIGNATURE 	DATE 2/10/06

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

**APPEARS THIS WAY
ON ORIGINAL**

ACTION PACKAGE CHECKLIST

BLA # NDA # 21-993	BLA STN# NDA Supplement #	If NDA, Efficacy Supplement Type
Proprietary Name: Claritin RediTabs 12 Hour Established Name: 5 mg loratadine Dosage Form: orally disintegrating tablets		Applicant: Schering-Plough HealthCare Products
RPM: Neel Patel		Division: DNCE Phone # 301-796-0970
<p>NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p>		<p>505(b)(2) NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p><input type="checkbox"/> If no listed drug, check here and explain:</p> <p>Review and confirm the information previously provided in Appendix B to the Regulatory Filing Review. Use this Checklist to update any information (including patent certification information) that is no longer correct.</p> <p><input type="checkbox"/> Confirmed <input type="checkbox"/> Corrected Date:</p>
❖ User Fee Goal Date		December 13, 2006
❖ Action Goal Date (if different)		
❖ Actions		
• Proposed action		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA <input type="checkbox"/> CR
• Previous actions (<i>specify type and date for each action taken</i>)		<input checked="" type="checkbox"/> None
❖ Advertising (<i>approvals only</i>) Note: If accelerated approval (21 CFR 314.510/601.41), advertising must have been submitted and reviewed (<i>indicate dates of reviews</i>)		<input type="checkbox"/> Requested in AP letter <input type="checkbox"/> Received and reviewed

❖ Application Characteristics	
Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): Type 5 NDAs, BLAs and Supplements: <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> CMA Pilot 1 <input type="checkbox"/> CMA Pilot 2 <input type="checkbox"/> Orphan drug designation NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart H <input type="checkbox"/> Approval based on animal studies NDAs and NDA Supplements: <input checked="" type="checkbox"/> OTC drug Other: Other comments:	
❖ Application Integrity Policy (AIP)	
<ul style="list-style-type: none"> Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> This application is on the AIP <ul style="list-style-type: none"> Exception for review (<i>file Center Director's memo in Administrative Documents section</i>) OC clearance for approval (<i>file communication in Administrative Documents section</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> Not an AP action
❖ Public communications (approvals only)	
<ul style="list-style-type: none"> Office of Executive Programs (OEP) liaison has been notified of action 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> Press Office notified of action 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> Indicate what types (if any) of information dissemination are anticipated 	<input checked="" type="checkbox"/> None <input type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

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)?

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 section below (Summary Reviews).

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

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) 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 section below (Summary Reviews).

If "No," continue with question (5).

- (5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) 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

<p>within the 45-day period).</p> <p><i>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 section below (Summary Reviews).</i></p> <p><i>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.</i></p>	
<p>Summary Reviews</p>	
<p>❖ Summary Reviews (e.g., Office Director, Division Director) (indicate date for each review)</p>	<p>DD- 12/5/06</p>
<p>❖ BLA approvals only: Licensing Action Recommendation Memo (LARM) (indicate date)</p>	
<p>Labeling</p>	
<p>❖ Package Insert</p>	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	
<p>❖ Patient Package Insert</p>	
<ul style="list-style-type: none"> • Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	
<p>❖ Medication Guide</p>	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling) 	
<p>❖ Labels (full color carton and immediate-container labels)</p>	
<ul style="list-style-type: none"> • Most-recent division-proposed labels (only if generated after latest applicant submission) 	
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling 	<p>October 4, 2006</p>

❖ Labeling reviews and minutes of any labeling meetings (<i>indicate dates of reviews and meetings</i>)	<input checked="" type="checkbox"/> DMETS November 17, 2006 <input type="checkbox"/> DSRCS <input type="checkbox"/> DDMAC <input type="checkbox"/> SEALD <input checked="" type="checkbox"/> Other reviews IDS: August 16 and 22, September 14, October 12, 2006, and November 21, 2006 <input type="checkbox"/> Memos of Mtgs
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Administrative Documents	
❖ Administrative Reviews (RPM Filing Review/Memo of Filing Meeting; ADRA) (<i>indicate date of each review</i>)	RPM- 10/13/06 CHM- 4/7/06 Clinpharm- 4/17/06 MO- 4/14/06 Pharmtox- 5/2/06
❖ NDA and NDA supplement approvals only: Exclusivity Summary (<i>signed by Division Director</i>)	<input checked="" type="checkbox"/> Included
❖ AIP-related documents <ul style="list-style-type: none"> Center Director's Exception for Review memo If AP: OC clearance for approval 	
❖ Pediatric Page (all actions)	<input checked="" type="checkbox"/> Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent. (<i>Include certification.</i>)	<input checked="" type="checkbox"/> Verified, statement is acceptable
❖ Postmarketing Commitment Studies <ul style="list-style-type: none"> Outgoing Agency request for post-marketing commitments (<i>if located elsewhere in package, state where located</i>) Incoming submission documenting commitment 	<input checked="" type="checkbox"/> None
❖ Outgoing correspondence (letters including previous action letters, emails, faxes, telecons)	See Outgoing Correspondence tab
❖ Internal memoranda, telecons, email, etc.	See Memo to File tab
❖ Minutes of Meetings <ul style="list-style-type: none"> Pre-Approval Safety Conference (<i>indicate date; approvals only</i>) Pre-NDA/BLA meeting (<i>indicate date</i>) EOP2 meeting (<i>indicate date</i>) Other (e.g., EOP2a, CMC pilot programs) 	<input checked="" type="checkbox"/> No mtg <input checked="" type="checkbox"/> No mtg PIND Meeting: January 5, 2005
❖ Advisory Committee Meeting <ul style="list-style-type: none"> Date of Meeting 48-hour alert or minutes, if available 	<input checked="" type="checkbox"/> No AC meeting
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	
CMC/Product Quality Information	
❖ CMC/Product review(s) (<i>indicate date for each review</i>)	November 29, 2006
❖ Reviews by other disciplines/divisions/Centers requested by CMC/product reviewer (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ BLAs: Product subject to lot release (APs only)	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Environmental Assessment (check one) (original and supplemental applications) <ul style="list-style-type: none"> <input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>) 	See page 46 of chemist review

• <input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>)	
• <input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>)	
❖ NDAs: Microbiology reviews (sterility & apyrogenicity) (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not a parenteral product
❖ Facilities Review/Inspection	
❖ NDAs: Facilities inspections (include EER printout)	Date completed: June 16, 2006 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation

❖ BLAs: Facility-Related Documents <ul style="list-style-type: none"> • Facility review (<i>indicate date(s)</i>) • Compliance Status Check (approvals only, both original and supplemental applications) (<i>indicate date completed, must be within 60 days prior to AP</i>) 	<input type="checkbox"/> Requested <input type="checkbox"/> Accepted <input type="checkbox"/> Hold
❖ NDAs: Methods Validation	<input checked="" type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed
Nonclinical Information	
❖ Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	September 19, 2006
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	
❖ Nonclinical inspection review Summary (DSI)	<input checked="" type="checkbox"/> None requested
Clinical Information	
❖ Clinical review(s) (<i>indicate date for each review</i>)	September 19, 2006
❖ Financial Disclosure reviews(s) or location/date if addressed in another review	Page 11 of review
❖ Clinical consult reviews from other review disciplines/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Microbiology (efficacy) reviews(s) (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not needed
❖ Safety Update review(s) (<i>indicate location/date if incorporated into another review</i>)	Page 34 of review
❖ Risk Management Plan review(s) (including those by OSE) (<i>indicate location/date if incorporated into another review</i>)	Page 41 of review
❖ Controlled Substance Staff review(s) and recommendation for scheduling (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not needed
❖ DSI Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input type="checkbox"/> None requested
• Clinical Studies	
• Bioequivalence Studies	November 17, 2006
• Clin Pharm Studies	
❖ Statistical Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None October 18, and November 29, 2006

Appendix A to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's Office of Regulatory Policy representative.

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/s/

Neel Patel
12/12/2006 02:16:56 PM

OTC Drug Labeling Review

Division of Over-The-Counter Drug Products (HFD-560)

Center for Drug Evaluation and Research • Food and Drug Administration

NDA Consultation Response Review

NDA # 21-993

Received Date: 11/17/06

Review Date: 11/21/06

Applicant: Schering-Plough HealthCare Products
556 Morris Avenue
Summit, New Jersey 07901-1330

Drug: Claritin RediTabs, 12 Hour Tablets
Loratadine, 5 mg (orally disintegrating tablets)

Pharmacologic Category: Antihistamine

Background:

On November 17, 2006, the Division of Medication Errors and Technical Support (DMETS) sent a memo to the Division of Nonprescription Clinical Evaluation in response to the Division's request that DMETS assess the descriptor "12 Hour" in conjunction with the proprietary name, Claritin RediTabs. This request was in regard to the potential name confusion with other proprietary or established drug names. Container label and carton labeling were provided for review and comment from a medication error perspective.

Reviewer Comments:

Based on the comments and recommendations included in the DMETS memo, this reviewer has the following comments.

- a. Most of DMETS comments have been addressed in the agency's subsequent communication with the sponsor and in subsequent draft labeling submitted to the agency.
- b. Concur with DMETS comments that the descriptor "12 Hour" should appear in close proximity wherever the phrase "Claritin Reditabs" appears on all carton SKUs, including side and back carton panels. The "12 Hour" modifier will help avoid possible consumer confusion with the sponsor's "24 Hour" product. However, this revision can be done post-approval.

Recommendation:

1. Labeling for this NDA can be approved as noted in the labeling review of 10/12/06.
2. Inform the sponsor to further revise the carton label for the 10-, 30-, 40-count carton labels and the 5- and 10-count alternate graphics carton labels to include the descriptor "12 Hour" in close proximity wherever the phrase "Claritin Reditabs" appears. The agency believes that the "12 Hour" modifier will help avoid possible consumer confusion with the sponsor's "24 Hour" Claritin drug product. Accordingly, this revision must occur within 180 days or at the time of next printing, whichever occurs first.

Cazemiro R. Martin
Reg. Review Chemist/IDS

Concur: Marina Chang, R.Ph.
Team Leader

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this page is the manifestation of the electronic signature.**

/s/

Cazemiro Martin
11/21/2006 02:47:19 PM
INTERDISCIPLINARY

Marina Chang
11/21/2006 03:00:08 PM
INTERDISCIPLINARY

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: November 17, 2006

FROM: John A. Kadavil, Ph.D.
Division of Scientific Investigations (HFD-48)

THROUGH: C.T. Viswanathan, Ph.D. _____
Associate Director - Bioequivalence
Division of Scientific Investigations (HFD-48)

SUBJECT: Review of EIR Covering NDA 21-993, Claritin®
RediTabs® 12 Hour (5 mg Loratidine) Orally
Disintegrating Tablets, sponsored by Schering-Plough
HealthCare Products

TO: Andrea Leonard Segal, M.D.
Director (Acting)
Division of Nonprescription Clinical Evaluation
(DNCE)

At the request of DNCE, the Division of Scientific Investigations conducted an audit of the analytical portions of the following bioequivalence studies:

Study CL2005-02: A Single Dose, Comparative, Randomized, Two-Way Crossover Bioequivalence Study of Loratidine 5 mg Administered as a Claritin® RediTabs® Tablet and as a Claritin-D® 12 Hour Extended Release Tablet

Study CL2004-01: A Single Dose, Comparative, Randomized, Crossover, Bioequivalence Study of Two 5 mg Claritin® RediTabs® Tablets and One 10 mg Claritin® RediTabs® Tablet

The analytical portions of these studies were conducted at _____ DNCE did not request inspection of the clinical portion of the study. Following the inspection at _____, Form 483 was issued. Our evaluation of the objectionable items are as follows:

1. Analytical runs were accepted even though more than 50% (2 out of 3) of the low QCs failed. Examples include the following:

- a. Study CL2005-02: Run 27EYO-A-2 for desloratadine (SCH 34117)
- b. Study CL2004-01: Run 12JGO-1-A for loratadine (SCH 29851) and runs 10JGO-2-A and 17JGO-2-B for desloratadine (SCH 34117).

Since > 50% of the low QCs were inaccurate (i.e., > ±15% of the intended concentration) in the aforementioned analytical runs, the accuracy of the runs cannot be assured. The firm's run acceptance criterion¹, requiring only 33% (1 of 3) QCs to pass at each level, is not acceptable. Due to inaccuracy of the analytical runs, data from the following subject samples (corresponding subjects are provided) analyzed in the runs should be excluded from the bioequivalence determination:

Analyte	Run	Subjects	Samples
Loratadine	12JGO-1-A	7, 31, 32, 33	314,1381-1398,1400-1438,1440-1494
Desloratadine	27EYO-A-2	79, 80, 81	3589-3726
	10JGO-2-A	25, 26, 27	1105-1139, 1141-1242
	17JGO-2-B	46, 47, 48	2071-2208

- 2. The sponsor did not provide objective criteria for selecting samples for pharmacokinetic (PK) repeat. Also, the reported results for sponsor-requested PK repeats ignored the original result and only compared the repeat results (re-assayed in triplicate). — followed the reporting procedures provided by the sponsor.

While the sponsor's procedures are not acceptable, less than 2% of the samples were re-assayed as PK repeats. The repeat and original results were included in both final reports in Tables 7 and 8 (CL2005-02) and Tables 12-15 (CL2004-01). It should be noted that >50% of the repeat results were within 20% of the original value for Project EYO, and 64% of the repeat results were within 20% of the original value for Project JGO.

¹ Schering Plough provided — the run acceptance criteria for the study.

Conclusions:

Following our evaluation of the inspectional findings, DSI recommends that the data for the following subjects from analytical runs with failing QC results be **excluded** from bioequivalence determination:

- Study CL2005-02
 - o Desloratadine: Subjects 7 (Period II, 10 hr sample), 79, 80 and 81

- Study CL2004-01
 - o Loratadine: Subjects 31, 32 and 33
 - o Desloratadine: Subjects 25, 26, 27, 46, 47 and 48

After you have reviewed this transmittal memo, please append it to the original NDA submission.

John A. Kadavil, Ph.D.

Final Classification: VAI ()

cc:
HFD-45/RF
HFD-48/Himaya/Kadavil/CF
DNCE/Abraham (via DFS)
HFR-CE2545/Milazzo
Draft: JAK 11/9/06
Edit: SS 11/9/06
DSI: O:\BE\eircover\21993sch.lor.doc
FACTS:

**This is a representation of an electronic record that was signed electronically and
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/s/

Amalia Himaya

11/17/2006 10:58:13 AM

CSO

Paper copy signed by Dr. Viswanathan on 11/17/06 and
available upon request.

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 21-993

Supplement #

Efficacy Supplement Type SE-

Trade Name: Claritin RediTabs 12 Hour

Established Name: loratadine

Strengths: 5 mg

Applicant: Schering-Plough HealthCare Products

Agent for Applicant: Date of Application: February 10, 2006

Date of Receipt: February 13, 2006

Date clock started after UN:

Date of Filing Meeting: April 5, 2006

Filing Date: April 14, 2006

Action Goal Date (optional):

User Fee Goal Date: December 13, 2006

Indication(s) requested: temporary relief of symptoms of runny nose, itchy, watery eyes, sneezing, and itching of the nose or throat, due to hay fever or other upper respiratory allergies

Type of Original NDA: (b)(1) (b)(2)

OR

Type of Supplement: (b)(1) (b)(2)

NOTE:

(1) If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). If the application is a (b)(2), complete Appendix B.

(2) If the application is a supplement to an NDA, please indicate whether the NDA is a (b)(1) or a (b)(2) application:

NDA is a (b)(1) application OR NDA is a (b)(2) application

Therapeutic Classification: S P
Resubmission after withdrawal? Resubmission after refuse to file?
Chemical Classification: (1,2,3 etc.) 5
Other (orphan, OTC, etc.) OTC

Form 3397 (User Fee Cover Sheet) submitted: YES NO

User Fee Status: Paid Exempt (orphan, government)
Waived (e.g., small business, public health)

NOTE: If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required. The applicant is required to pay a user fee if: (1) the product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the product described in the application. Highlight the differences between the proposed and approved labeling.

Version: 12/15/2004

This is a locked document. If you need to add a comment where there is no field to do so, unlock the document using the following procedure. Click the 'View' tab; drag the cursor down to 'Toolbars'; click on 'Forms.' On the forms toolbar, click the lock/unlock icon (looks like a padlock). This will allow you to insert text outside the provided fields. The form must then be relocked to permit tabbing through the fields.

If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the user fee staff.

- Is there any 5-year or 3-year exclusivity on this active moiety in an approved (b)(1) or (b)(2) application? YES NO
If yes, explain:
- Does another drug have orphan drug exclusivity for the same indication? YES NO
- If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? YES NO

If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

- Is the application affected by the Application Integrity Policy (AIP)? YES NO
If yes, explain:
- If yes, has OC/DMPQ been notified of the submission? YES NO
- Does the submission contain an accurate comprehensive index? YES NO
- Was form 356h included with an authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. agent must sign.
- Submission complete as required under 21 CFR 314.50? YES NO
If no, explain:
- If an electronic NDA, does it follow the Guidance? N/A YES NO
If an electronic NDA, all forms and certifications must be in paper and require a signature.
Which parts of the application were submitted in electronic format?

Additional comments:

- If an electronic NDA in Common Technical Document format, does it follow the CTD guidance? N/A YES NO
- Is it an electronic CTD (eCTD)? N/A YES NO
If an electronic CTD, all forms and certifications must either be in paper and signed or be electronically signed.

Additional comments:

- Patent information submitted on form FDA 3542a? YES NO
- Exclusivity requested? YES, _____ Years NO
NOTE: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.
- Correctly worded Debarment Certification included with authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. Agent must sign the certification.

NOTE: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e., “[Name of applicant] 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.” Applicant may not use wording such as “To the best of my knowledge”

- Financial Disclosure forms included with authorized signature? YES NO
(Forms 3454 and 3455 must be included and must be signed by the APPLICANT, not an agent.)
NOTE: Financial disclosure is required for bioequivalence studies that are the basis for approval.
- Field Copy Certification (that it is a true copy of the CMC technical section)? Y NO
- PDUFA and Action Goal dates correct in COMIS? YES NO
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.
- List referenced IND numbers: PIND 63,797
- End-of-Phase 2 Meeting(s)? Date(s) _____ NO
If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s)? Date(s) February 3, 2005 (PIND meeting) NO
If yes, distribute minutes before filing meeting.

Project Management

- Was electronic “Content of Labeling” submitted? YES NO
If no, request in 74-day letter.
- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC? YES NO
- Risk Management Plan consulted to ODS/IO? N/A YES NO
- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS? Y NO
- MedGuide and/or PPI (plus PI) consulted to ODS/DSRCS? N/A YES NO
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted? N/A YES NO

If Rx-to-OTC Switch application:

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/DSRCS? N/A YES NO
- Has DOTCDP been notified of the OTC switch application? YES NO

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff?
YES NO

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES NO
If no, did applicant submit a complete environmental assessment? YES NO
If EA submitted, consulted to Florian Zielinski (HFD-357)? YES NO
- Establishment Evaluation Request (EER) submitted to DMPQ? YES NO
- If a parenteral product, consulted to Microbiology Team (HFD-805)? YES NO

**APPEARS THIS WAY
ON ORIGINAL**

ATTACHMENT

MEMO OF FILING MEETING

DATE: April 6, 2006

BACKGROUND:

Schering-Plough Healthcare Products has submitted NDA 21-993 to market a new orally disintegrating 5 mg loratadine tablet dosage strength. This product would be marketed under the proposed tradename Claritin Reditabs 12 Hour and carry the same indications as the currently marketed Claritin 10mg orally disintegrating tablet dosage strength.

ATTENDEES: Neel Patel, Steve Osborne, Davia Shetty, Andrea Leonard-Segal, Cazemiro Martin, Marina Chang, Shinja Kim, Larry Sancilio, John Kadavil, Shulin Ding, Emmanuel Fadiran, Joe Sun, Tarun Mehta,

ASSIGNED REVIEWERS (including those not present at filing meeting) :

<u>Discipline</u>	<u>Reviewer</u>
Medical:	Steve Osborne
Secondary Medical:	
Statistical:	
Pharmacology:	Larry Sancilio
Statistical Pharmacology:	
Chemistry:	Tarun Mehta
Environmental Assessment (if needed):	
Biopharmaceutical:	Shinja Kim
Microbiology, sterility:	
Microbiology, clinical (for antimicrobial products only):	
DSI:	John Kadavil
Regulatory Project Management:	Neel Patel
Other Consults:	Cazemiro Martin – labeling

Per reviewers, are all parts in English or English translation? YES NO
If no, explain:

CLINICAL FILE REFUSE TO FILE

- Clinical site inspection needed? YES NO
- Advisory Committee Meeting needed? YES, date if known _____ NO
- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? N/A YES NO

CLINICAL MICROBIOLOGY	N/A <input checked="" type="checkbox"/>	FILE <input type="checkbox"/>	REFUSE TO FILE <input type="checkbox"/>
STATISTICS	N/A <input checked="" type="checkbox"/>	FILE <input type="checkbox"/>	REFUSE TO FILE <input type="checkbox"/>
BIOPHARMACEUTICS		FILE <input checked="" type="checkbox"/>	REFUSE TO FILE <input type="checkbox"/>

- Biopharm. inspection needed? YES NO

PHARMACOLOGY N/A FILE REFUSE TO FILE

- GLP inspection needed? YES NO

CHEMISTRY FILE REFUSE TO FILE

- Establishment(s) ready for inspection? YES NO
- Microbiology YES NO

ELECTRONIC SUBMISSION:

Any comments:

REGULATORY CONCLUSIONS/DEFICIENCIES:
(Refer to 21 CFR 314.101(d) for filing requirements.)

- The application is unsuitable for filing. Explain why:
- The application, on its face, appears to be well-organized and indexed. The application appears to be suitable for filing.
 - No filing issues have been identified.
 - Filing issues to be communicated by Day 74. List (optional):

ACTION ITEMS:

1. If RTF, notify everybody who already received a consult request of RTF action. Cancel the EER.
2. If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
3. Convey document filing issues/no filing issues to applicant by Day 74.

Neel Patel
Regulatory Project Manager, HFD-560

Appendix A to NDA Regulatory Filing Review

An application is likely to be a 505(b)(2) application if:

- (1) it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)
- (2) it relies on the Agency's previous approval of another sponsor's drug product (which may be evidenced by reference to publicly available FDA reviews, or labeling of another drug sponsor's drug product) to meet any of the approval requirements (unless the application includes a written right of reference to data in the other sponsor's NDA)
- (3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)
- (4) it seeks approval for a change from a product described in an OTC monograph and relies on the monograph to establish the safety or effectiveness of one or more aspects of the drug product for which approval is sought (see 21 CFR 330.11).

Products that may be likely to be described in a 505(b)(2) application include combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations), OTC monograph deviations, new dosage forms, new indications, and new salts.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, please consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

**Appendix B to NDA Regulatory Filing Review
Questions for 505(b)(2) Applications**

1. Does the application reference a listed drug (approved drug)? YES NO

If "No," skip to question 3.

2. Name of listed drug(s) referenced by the applicant (if any) and NDA/ANDA #(s):
3. The purpose of this and the questions below (questions 3 to 5) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval and that should be referenced as a listed drug in the pending application.

- (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved? YES NO

(Pharmaceutical equivalents are drug products in identical dosage forms that: (1) contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; (2) do not necessarily contain the same inactive ingredients; and (3) meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. (21 CFR 320.1(c))

If "No," skip to question 4. Otherwise, answer part (b).

- (b) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)? YES NO
(The approved pharmaceutical equivalent(s) should be cited as the listed drug(s).)

If "Yes," skip to question 6. Otherwise, answer part (c).

- (c) Have you conferred with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007)? YES NO

If "No," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.

4. (a) Is there a pharmaceutical alternative(s) already approved? YES NO

(Pharmaceutical alternatives are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)

If "No," skip to question 5. Otherwise, answer part (b).

- (b) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)? YES NO
(The approved pharmaceutical alternative(s) should be cited as the listed drug(s).)

NOTE: *If there is more than one pharmaceutical alternative approved, consult the Director, Division of*

Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007) to determine if the appropriate pharmaceutical alternatives are referenced.

If "Yes," skip to question 6. Otherwise, answer part (c).

- (c) Have you conferred with the Director, Division of Regulatory Policy II, ORP? YES NO

If "No," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.

5. (a) Is there an approved drug product that does not meet the definition of "pharmaceutical equivalent" or "pharmaceutical alternative," as provided in questions 3(a) and 4(a), above, but that is otherwise very similar to the proposed product? YES NO

If "No," skip to question 6.

If "Yes," please describe how the approved drug product is similar to the proposed one and answer part (b) of this question. Please also contact the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007), to further discuss.

- (b) Is the approved drug product cited as the listed drug? YES NO
6. Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution").
7. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA will refuse-to-file such NDAs (see 21 CFR 314.101(d)(9)).) YES NO
8. Is the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application should be refused for filing under 21 CFR 314.101(d)(9). YES NO
9. Is the rate at which the product's active ingredient(s) is absorbed or otherwise made available to the site of action unintentionally less than that of the RLD (see 21 CFR 314.54(b)(2))? If yes, the application should be refused for filing under 21 CFR 314.101(d)(9). YES NO
10. Are there certifications for each of the patents listed for the listed drug(s)? YES NO
11. Which of the following patent certifications does the application contain? (Check all that apply and identify the patents to which each type of certification was made, as appropriate.)
- 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)
Patent number(s):
- 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)
Patent number(s):

- 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)
Patent number(s):
- 21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted. (Paragraph IV certification)
Patent number(s):

NOTE: IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must **subsequently** submit a signed certification stating that the NDA holder and patent owner(s) were notified the NDA was filed [21 CFR 314.52(b)]. The applicant must also submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)].

- 21 CFR 314.50(i)(1)(ii): No relevant patents.
- 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)
Patent number(s):
- 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above).
Patent number(s):
- Written statement from patent owner that it consents to an immediate effective date upon approval of the application.
Patent number(s):

12. Did the applicant:

- Identify which parts of the application rely on information (e.g. literature, prior approval of another sponsor's application) that the applicant does not own or to which the applicant does not have a right of reference?
YES NO
- Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity?
YES NO
- Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug?
N/A YES NO
- Certify that it is seeking approval only for a new indication and not for the indications approved for the listed drug if the listed drug has patent protection for the approved indications and the applicant is requesting only the new indication (21 CFR 314.54(a)(1)(iv).)?
N/A YES NO

13. If the (b)(2) applicant is requesting 3-year exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):

- Certification that at least one of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a). YES NO

- A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval. YES NO

- EITHER

The number of the applicant's IND under which the studies essential to approval were conducted.

IND# _____ NO

OR

A certification that the NDA sponsor provided substantial support for the clinical investigation(s) essential to approval if it was not the sponsor of the IND under which those clinical studies were conducted?

YES NO

14. Has the Associate Director for Regulatory Affairs, OND, been notified of the existence of the (b)(2) application?

YES NO

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/s/

Neel Patel
10/13/2006 03:29:33 PM
CSO

OTC Drug Labeling Review

Division of Over-The-Counter Drug Products (HFD-560)

Center for Drug Evaluation and Research • Food and Drug Administration

NDA Labeling 2nd Amendment Review

NDA # 21-993

Submission Date: 10/2/06, 10/3/06, and 10/4/06

Review Date: 10/12/06

Applicant: Schering-Plough HealthCare Products
556 Morris Avenue
Summit, New Jersey 07901-1330
(908) 473-1741

Applicant's Representative: Nancy Pierro
Regulatory Affairs Manager

Drug: Claritin RediTabs, 12 Hour Tablets
Loratadine, 5 mg (orally disintegrating tablets)

Pharmacologic Category: Antihistamine

Submitted:

1. Letter of Commitment re. Blister Foil Artwork (submitted on 10/2/06)
2. Revised draft labeling (10/3/06 - hard copy and 10/4/06 – electronic submission) provided for:
 - 10-, 30-, and 40-count cartons
 - 5- and 10-count alternate graphics carton
 - 5- and 10-count blister foil [to be implemented no later than 6 months from receipt of approval of the application]
 - Annotated Drug Facts specifications for all SKUs included in this submission

Background:

In response to the Agency's labeling comments dated 10/21/06, the sponsor submitted on 9/8/06 draft labeling for the 10-count carton and 5- and 10-count blister card, along with annotated specifications for its draft 10-count carton Drug Facts labeling. This reviewer has reviewed the 9/8/06 submission on 9/14/06 (see DFS review).

Subsequently, the sponsor has submitted a letter of commitment dated 10/2/06, concerning its 5- and 10-count blister card labeling. In this letter, the sponsor commits to the following:

- The blister foil artwork originally submitted on 2/10/06 and resubmitted on 6/20/06 will be discontinued no later than six months from receipt of approval of the application.
- The blister foil artwork originally submitted on 9/8/06 and resubmitted on 10/4/06 will be implemented no later than six months from receipt of approval of the application.

In addition, the sponsor submitted on 10/3/06 (hard copy submission of labels) and 10/4/06 (electronic submissions of labels) as stated above.

Reviewer Comments:

A. **Carton labels:** [10-, 30-, and 40-count cartons, and 5- and 10-count alternate graphics cartons]

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- The labeling and the annotated Drug Facts specifications for these SKUs are acceptable.

B. **Blister card labels:** [5- and 10-count]

C. **Sponsor's Letter of Commitment:** Acceptable

Recommendations:

1. The draft labeling and annotated Drug Facts specifications submitted on 10/4/06 (electronic submission) for the 10-, 30-, and 40-count cartons, and the 5- and 10-count alternate graphics cartons are acceptable.
2. In the letter of commitment dated 10/2/06, the sponsor commits to the following:
 - The blister foil artwork originally submitted on 2/10/06 and resubmitted on 6/20/06 will be discontinued no later than six months from receipt of approval of the application.
 - The blister foil artwork originally submitted on 9/8/06 and resubmitted on 10/4/06 will be implemented no later than six months from receipt of approval of the application.The terms of this commitment are acceptable.
3. An approval letter can be issued to the sponsor requesting final printed labels for the following:
 - A. 10-, 30-, and 40-count cartons, and the 5- and 10-count alternate graphics cartons that are identical to the labeling and annotated Drug Facts specifications submitted on 10/4/06.
 - B. 5- and 10-count blister cards that are identical to the labeling submitted on the following dates:
 - a. 2/10/06 and resubmitted on 6/20/06. (Note: As the sponsor indicated, these blister card labels will be discontinued six months from receipt of approval of the application.)
 - b. 9/8/06 and resubmitted on 10/4/06. (Note: As the sponsor indicated, these blister card labels will be implemented no later than six months from receipt of approval of the application.)
4. Inform the sponsor that the flag "New 12 Hour!" on the 5- and 10-count alternate graphics cartons must be deleted from the PDP six months after introduction into the market place.

Cazemiro R. Martin
Reg. Review Chemist/IDS

Concur: Marina Chang, R.Ph.
Team Leader

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/s/

Cazemiro Martin
10/12/2006 02:37:07 PM
INTERDISCIPLINARY

Marina Chang
10/12/2006 02:43:33 PM
INTERDISCIPLINARY

MEMORANDUM OF TELECON

DATE: September 11, 2006

APPLICATION NUMBER: NDA 21-993, Claritin RediTabs 12 Hour (Loratadine) orally disintegrating tablets, 5 mg

BETWEEN:

Name: Joyce Yates - Director, Regulatory Affairs (Summit, NJ)
Doreen Frank - Director, Regulatory Affairs (Summit, NJ)
Nancy Pierro - Manager, Regulatory Affairs (Summit, NJ)
Chris Rainey - Director, Analytical Stability (Memphis, TN)
Bill McLaughlin - Fellow, Pharmaceutical Research (Memphis, TN)
Mike Tune - Director, Packaging Services & Technology (Memphis, TN)
Phone: 888-560-9748, pass code 693797
Representing: **Schering-Plough HealthCare Products**

Representing: **Schering-Corporation**
Rosie McLaughlin - Technical Director, Zydis (Swindon, UK)
Tony Engel - Manager, Analytical Services (Swindon, UK)
Representing: **Cardinal Health**

AND

Name: Tarun Mehta, M.Sc, Chemist
Shulin Ding, Ph.D., Pharmaceutical Assessment Lead
Linda Athey, Regulatory Project Manager for Quality
Division of Pre-Marketing Assessment II, Branch III

SUBJECT: Clarification of Information Request Letter dated August 8, 2006.

BACKGROUND:

FDA sent a CMC Information Request Letter dated August 8, 2006 requesting clarification and information.

CALL: At the request of the reviewing chemist, Tarun Mehta, and concurrence of the Branch Chief, FDA's Chemist for Dermatology and Dental, Mr. Mehta conveyed the following:

QUESTION 1;

In Section: P.2.3, Manufacturing, please clarify the following manufacturing process:

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RESPONSE;

QUESTION 3;

RESPONSE;

Adequate response was submitted.

QUESTION 5;

RESPONSE;

The sponsor agrees with all other points covered in the Information Request Letter dated August 8, 2006, and will submit an amendment to the file and send an electronic copy to Linda Athey, FDA's Regulatory Health Project Manager for Quality.

{See appended electronic signature page}

Linda Athey
Regulatory Health Project Manager for Quality

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/s/

Linda D Mullins-Athey
10/2/2006 01:44:45 PM
PROJECT MANAGER FOR QUALITY

OTC Drug Labeling Review

Division of Over-The-Counter Drug Products (HFD-560)

Center for Drug Evaluation and Research • Food and Drug Administration

NDA Labeling Amendment Review

NDA # 21-993

Submission Date: 9/8/06

Review Date: 9/14/06

Applicant: Schering-Plough HealthCare Products
556 Morris Avenue
Summit, New Jersey 07901-1330
(908) 473-1741

Applicant's Representative: Nancy Pierro
Regulatory Affairs Manager

Drug: Claritin RediTabs, 12 Hour Tablets
Loratadine, 5 mg (orally disintegrating tablets)

Pharmacologic Category: Antihistamine

Submitted: Revised draft labeling provided for:

- 10-count carton
- 5- and 10-count blister card
- Annotated Drug Facts specifications

Background:

In response to the Agency's labeling comments dated August 21, 2006, the sponsor has submitted revised draft labeling for the 10-count carton and 5- and 10-count blister card, along with annotated specifications for its draft 10-count carton Drug Facts labeling. The sponsor has responded as follows to the Agency's August 21, 2006 labeling comments:

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Reviewer Comments:

A. Carton label (10-count):

- The labeling and the annotated Drug Facts specifications for this SKU are acceptable.

B. Blister card label (5- and 10-count):

Recommendations:

A. Inform the sponsor that:

1. The revised 10-count draft carton label can be approved. Also inform the sponsor that it will need to resubmit revised labeling for its other Claritin RediTab Tablets" SKUs (i.e., 30- and 40-count cartons, 5- and 10-count alternate graphics, and annotated Drug Facts specifications for each corresponding SKU) for agency pre-approval prior to the application PDUFA date.
2. The Drug Facts annotated specifications for the 10-count carton is acceptable.
3. The blister card labels for the 5- and 10-counts can be approved as follows:
 - (i) Labels submitted by sponsor on *February 10, 2006*: Approved for only 180 days after initially introduced into the market place.
 - (ii) Labels submitted by sponsor on *September 8, 2006*: Approved
4. A letter of commitment from the sponsor is needed to confirm that the Agency's labeling comments for the 5- and 10-count blister card labeling will be implemented no later than 6 months after the SKUs are initially introduced into the market place.

- B. Inquire of the sponsor if it intends to submit an additional revised 5-count blister foil labeling as it indicates in its cover letter. The Agency is not sure if there is an additional revised 5-count blister card labeling the sponsor intends to submit other than the 5- and 10-count blister card labeling included in this submission.

Cazemiro R. Martin
Reg. Review Chemist/IDS

Concur: Marina Chang, R.Ph.
Team Leader

**APPEARS THIS WAY
ON ORIGINAL**

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/s/

Cazemiro Martin
9/14/2006 09:33:55 AM
INTERDISCIPLINARY

Marina Chang
9/14/2006 11:03:45 AM
INTERDISCIPLINARY

OTC Drug Labeling Review

Division of Over-The-Counter Drug Products (HFD-560)

Center for Drug Evaluation and Research • Food and Drug Administration

NDA Memo to File

NDA # 21-993

Submission Date: 2/10/06, 6/16/06, 6/20/06

Review Date: 8/22/06

Applicant: Schering-Plough HealthCare Products
556 Morris Avenue
Summit, New Jersey 07901-1330
(908) 473-1741

Applicant's
Representative: Doreen Frank
Director, Regulatory Affairs

Drug: Claritin RediTabs, 12 Hour Tablets
Loratadine, 5 mg

Pharmacologic Category: Antihistamine

Submitted: Draft labeling provided for:

- 5-, 10-, and 30-count carton (2/2/06); and 40-count carton (6/16/06)
- 5- and 10-count alternate graphic carton
- 5- and 10-count blister card
- Annotated Drug Facts specifications

Correction:

In the "Background" discussion of the labeling review dated August 16, 2006, the reference to "February 2, 2006" is corrected to read "February 10, 2006".

Cazemiro R. Martin
Reg. Review Chemist/IDS

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/s/

Cazemiro Martin
8/22/2006 07:38:59 AM
INTERDISCIPLINARY



NDA 21-993

DISCIPLINE REVIEW LETTER

Schering-Plough HealthCare Products
Attention: Nancy Pierro
Manager, Regulatory Affairs
556 Morris Avenue
Summit, New Jersey 07901

Dear Ms. Pierro:

Please refer to your February 10, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for for Claritin RediTabs 12 Hour (5 mg loratadine) orally disintegrating tablets.

We acknowledge receipt of your submissions dated February 10, June 16 and 20, 2006.

Our review of the labeling for your submission is complete, and we have identified the following deficiencies in your June 16 and 20, 2006 submissions:

A. Carton Label for all stock keeping units (SKUs)

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B. Blister Card

We are providing these comments to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

In order to ensure a timely action for this new drug application, we request that you respond to the issues listed above as soon as possible and submit a new label with these changes as an amendment to your February 10, 2006 submission.

Please cite the application number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Nonprescription Products
Division of Nonprescription Clinical Evaluation
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions you may contact Neel Patel, Regulatory Project Manager, at (301) 796-0970.

Sincerely,

{See appended electronic signature page}

Leah Christl, Ph.D.
Chief, Project Management Staff
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

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/s/

Leah Christl

8/21/2006 03:07:26 PM

OTC Drug Labeling Review

Division of Over-The-Counter Drug Products (HFD-560)

Center for Drug Evaluation and Research • Food and Drug Administration

NDA Labeling Review

NDA # 21-993

Submission Date: 2/10/06, 6/16/06, 6/20/06

Review Date: 8/16/06

Applicant: Schering-Plough HealthCare Products
556 Morris Avenue
Summit, New Jersey 07901-1330
(908) 473-1741

Applicant's Representative: Doreen Frank
Director, Regulatory Affairs

Drug: Claritin RediTabs, 12 Hour Tablets
Loratadine, 5 mg

Pharmacologic Category: Antihistamine

Submitted: Draft labeling provided for:

- 5-, 10-, and 30-count carton (2/2/06); and 40-count carton (6/16/06)
- 5- and 10-count alternate graphic carton
- 5- and 10-count blister card
- Annotated Drug Facts specifications

Background:

Schering Corporation is seeking approval to market Claritin RediTabs 12 Hour Tablets, an immediate release orally disintegrating dosage form containing 5 mg of loratadine. The proposed indication is for temporary relief of symptoms of allergic rhinitis. The dose for adults and children 6 years of age and over is one 5 mg orally disintegrating tablet every twelve hours.

The sponsor has previously submitted draft labeling in its February 2, 2006 and June 16, 2006 submissions. The sponsor indicated in its June 16, 2006 submission that the originally submitted 60-count SKU has been revised to a 40-count SKU.

This June 20, 2006 submission supersedes the previous two submissions and includes:

• ✓

According to the sponsor, the Claritin 5 mg orally disintegrating tablets will be packaged in 5- and 10-count: _____ blister cards and placed in fully labeled cartons.

Reviewer Comments:

1. Carton labeling: (5-, 10-, 30-, and 40-count SKUs; 5- and 10-count alternate graphic SKUs):



B. Flag "New 12 Hour!": This flag must be deleted from the PDP six months after introduction into the market place.

2. Blister card labeling: (5- and 10-count):



3. The annotated specifications for the **Drug Facts** format are acceptable for all SKUs.

Recommendations:

This application cannot be approved. Inform the sponsor to revise the labeling of the 5-, 10-, 30- and 60-count cartons, 5- and 10-count alternate graphic cartons, and the 5- and 10-count blister card as follows and resubmit revised labeling for all SKUs to the Agency for review:

1. All carton SKUs:



Cazemiro R. Martin
Reg. Review Chemist/IDS

Concur: Marina Chang, R.Ph.
Team Leader

**APPEARS THIS WAY
ON ORIGINAL**

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/s/

Cazemiro Martin
8/16/2006 08:09:14 AM
INTERDISCIPLINARY

Marina Chang
8/16/2006 08:35:05 AM
INTERDISCIPLINARY



NDA 21-993

INFORMATION REQUEST LETTER

Schering-Plough HealthCare Products
Attention: Doreen Frank
Associate Director, Regulatory Affairs
Three Connell Drive, PO Box 603
Berkeley Heights, NJ 07922-0603

Dear Ms. Frank:

Please refer to your February 10, 2006, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Claritin RediTabs 12 Hour (Loratadine) orally disintegrating tablets, 5 mg.

We also refer to your submission dated March 15 and April 11, 2006.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and request for additional information. We request a prompt written response in order to continue our evaluation of your NDA.

1. In Section: P.2.3 Manufacturing, please clarify the following manufacturing process:

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3.

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6.

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/s/

Moo-Jhong Rhee
8/8/2006 11:40:43 AM
Chief, Branch III



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-993

Schering-Plough HealthCare Products
Attention: Doreen Frank
Director, Regulatory Affairs
556 Morris Avenue
Summit, NJ 07901-1330

Dear Ms. Frank:

Please refer to your submission dated March 15, 2006, requesting a waiver for pediatric studies for Claritin RediTabs 12 Hour (5 mg loratadine) orally disintegrating tablets.

We have reviewed the submission and agree that a waiver is justified for Claritin RediTabs 12 Hour for the temporary relief of symptoms of runny nose, itchy, watery eyes, sneezing, and itching of the nose or throat, due to hay fever or other upper respiratory allergies for children under 2 years of age because this product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients, and is not likely to be used in a substantial number of pediatric patients. We note that you have fulfilled the pediatric study requirement for this application in children greater than 2 years of age.

Accordingly, at this time, a partial waiver for pediatric studies for your application is granted under section 2 of the Pediatric Research Equity Act.

If you have questions, contact Neel Patel, Regulatory Project Manager, at 301-796-0970.

Sincerely,

{See appended electronic signature page}

Andrea Leonard-Segal, MD

Director

Division of Nonprescription Clinical Evaluation

Office of Nonprescription Products

Center for Drug Evaluation and Research

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/s/

Andrea Segal

6/27/2006 03:50:03 PM

NDA Pharmacology Fileability Check List

NDA No: 21-993

Date of submission: 2/10/06

Date of Fileability meeting: 3/06/06

Information to Sponsor: Yes () No (X)

Date of check list: 5/1/06

(1) On its face, is the Pharm/Tox section of the NDA organized in a manner to allow substantive review? Yes (X) No () NA (). Reference was made to the information in NDAs 19-658 and 20-704.

(2) On its face, is the Pharm/Tox section of the NDA legible for review? Yes (X) No () NA (). Reference was made to the information in NDAs 19-658 and 20-704.

(3) Are final reports of all required and requested preclinical studies submitted in this NDA? Yes (X) No () NA () Reference was made to the information in NDAs 19-658 and 20-704.

	Yes	No	NA
Pharmacology	(X)	()	()
ADME	(X)	()	()
Toxicology (duration, route of administration and species specified)			
acute	(X)	()	()
subchronic and chronic studies	(X)	()	()
reproductive studies	(X)	()	()
carcinogenicity studies	(X)	()	()
mutagenicity studies	(X)	()	()
special studies	(X)	()	()
others	(X)	()	()

(4) If the formulation to be marketed is different from the formulation used in the toxicology studies, is repeating or bridging the studies necessary? Yes () No (X) NA ()

If no, state why not? This oral formulation contains approved excipients.

If yes, has the applicant made an appropriate effort to repeat the studies using the to be marketed product, to bridge the studies or to explain why such repetition or bridging should not be required? Yes () No () NA ().

(5) Are the proposed preclinical labeling sections (carcinogenesis, mutagenesis and impairment of fertility, pregnancy category and overdosage) appropriate (including human dose multiples expressed in either mg/m² or comparative systemic exposure levels) and in accordance with 201.57? Yes () No () NA (X). This is an OTC product and this type of labeling is not required.

(6) Has the applicant submitted all special studies/data requested by the Division prior to the submission including but not limited to pre-NDA discussion? Yes () No () NA (X)

(7) On its face, does the route of administration used in the pivotal toxicity studies appear to be the same as the intended clinical route? Yes (X) No () NA ()

If not, has the applicant submitted a rationale to justify the alternative route?
Yes () No () NA ()

(8) Has the applicant submitted a statement(s) that all of the toxicity studies have been performed in accordance with the GLP regulations (21 CFR 58) or an explanation for any significant deviations? Yes (X) No () NA () .

(9) Has the applicant submitted any studies or data to address any impurity or extractable issues (if any)? Yes () No () NA (X)

(10) Are there any outstanding preclinical issues? Yes () No (X)
If yes, identify those below.

(11) From a preclinical perspective, is this NDA fileable? Yes (X) No ().
If no, state below why it is not.

(12) Should any additional information/data be requested? Yes () No (X)

NDA Planning Timeline

NDA No.: 21-993

Date of planning timeline:

5/1/06

PDUFA Due Date:

12/13/06

Projected review completion date: 9/1/06

Milestone Dates

Pharmacology and ADME

Sept. 1, 2006

Toxicology

Sept. 1, 2006

General toxicity studies

Carcinogenicity studies and mutagenicity studies

a. Statistical consult request for CA studies

b. Submission of CA studies for CAC concurrence

Reproductive studies

Special studies and others

Labeling

NA

Signatures (optional):

Reviewer Signature _____

Lawrence F. Sancilio, Ph.D.

Supervisor Signature _____

C. Joseph Sun, Ph.D.

Concurrence Yes ___ **No** ___

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/s/

Lawrence Sancilio
5/1/2006 04:16:08 PM
PHARMACOLOGIST

Joseph Sun
5/2/2006 10:43:36 AM
PHARMACOLOGIST
I concur.

NDA 45 Day Fileability Meeting Checklist

NDA#: 21-993, S-000

Product Name: Claritin 5 mg Orally Disintegrating Tablets (RediTabs)

Sponsor: Schering-Plough HealthCare Products

Reviewer: Steven Osborne, M.D.

Date: 4/13/06

Item	Yes	No
1. Is the clinical section of the NDA organized in a manner to allow substantive review to begin?	X	
2. Is the clinical section of the NDA indexed and paginated in a manner to allow substantive review to begin?	X	
3. Is the clinical section of the NDA legible so that substantive review can begin?	X	
4. If needed, has the sponsor made an appropriate attempt to determine the most appropriate dosage and schedule for this product through appropriately designed dose-ranging studies?	X	
5. Do there appear to be the requisite number of adequately and well-controlled studies in the application?	X	
6. Are the pivotal efficacy studies of appropriate design to meet basic requirements for approvability of this product based on proposed draft labeling?	X	
7. Are all data sets for pivotal efficacy studies complete for all indications requested?	X	
8. Do all pivotal studies appear to be adequate and well-controlled within current divisional policies (or to the extent agreed to previously with the applicant by the Division) for approvability of this product based on proposed draft labeling?	X	
9. Has the applicant submitted line listings in a format to allow reasonable review of the patient data and in the format agreed to previously by the Division?	X	
10. Has the application submitted a rationale for the applicability of foreign data (disease specific, microbiologic specific) in the submission to the U.S. population?	X	
11. Has the applicant submitted all additional required case record forms, in addition to deaths and drop-outs, previously requested by the Division?	X	
12. Has the applicant presented the safety data in a manner consistent with Center guidelines and/or in a manner previously agreed to by the Division?	X	
13. Has the applicant presented the safety assessment based on all current world-wide knowledge regarding this product?		X
14. Has the applicant submitted adequate and well-controlled actual usage trial(s) within current divisional policies (or to the extent agreed to previously with the applicant by the Division) for approvability of this product based on proposed draft labeling?	X	
15. Has the applicant submitted adequate and well-controlled labeling comprehension trial(s) within current divisional policies (or to the extent agreed to previously with the applicant by the Division) for approvability of this product based on proposed draft labeling?		X

Item	Yes	No
16. Has the applicant submitted draft labeling consistent with 201.5 and 201.56, current divisional policies, and the design of the development package?	X	
17. Has the applicant submitted all special studies/data requested by the Division during pre-submission discussions with the sponsor?	X	
18. From a clinical perspective, is this NDA file-able? In no, please explain below.	X	

Reviewer Comments: The Sponsor will be asked to submit additional safety data

**APPEARS THIS WAY
ON ORIGINAL**

Medical Officer
Division of Over-the-Counter Drug Products

Medical Team Leader
Division of Over-the-Counter Drug Products

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/s/

Steven Osborne
4/13/2006 12:01:13 PM
MEDICAL OFFICER

Daiva Shetty
4/14/2006 09:15:18 AM
MEDICAL OFFICER



NDA 21-993

NDA ACKNOWLEDGMENT

Schering-Plough HealthCare Products
Attention: Doreen Frank
Director, Regulatory Affairs
556 Morris Avenue
Summit, NJ 07901-1330

Dear Ms. Frank:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Claritin RediTabs 12 Hour (5 mg loratadine) orally
disintegrating tablets

Review Priority Classification: Standard (S)

Date of Application: February 10, 2006

Date of Receipt: February 13, 2006

Our Reference Number: NDA 21-993

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on April 14, 2006 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be December 13, 2006.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not fulfilled the requirements. We acknowledge receipt of your request for a waiver of pediatric studies for this application. Once the application has been filed we will notify you whether we have waived the pediatric study requirement for this application.

Please cite the NDA number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

NDA 21-993

Page 2

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Nonprescription Products
Division of Nonprescription Clinical Evaluation
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions, call Neel Patel, Regulatory Project Manager, at (301) 796-0970.

Sincerely,

{See appended electronic signature page}

Leah Christl, Ph.D.
Acting Chief, Project Management Staff
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

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/s/

Leah Christl

4/4/2006 04:09:58 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

**PRESCRIPTION DRUG USER FEE
COVERSHEET**

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>

<p>1. APPLICANT'S NAME AND ADDRESS</p> <p>SCHERING PLOUGH HEALTHCARE PRODUCTS INC Doreen Frank Schering-Plough HealthCare Products 556 Morris Avenue Summit NJ 07901-1330 US</p>	<p>4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER</p> <p>21-993</p>
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<p>2. TELEPHONE NUMBER</p> <p>908-473-1655</p>	<p>5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?</p> <p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p> <p>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:</p> <p><input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION</p> <p><input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:</p> <p>19-670, 20-704</p>
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<p>3. PRODUCT NAME</p> <p>Claritin RediTabs 12 Hour Tablets (loratadine, 5 mg)</p>	<p>6. USER FEE I.D. NUMBER</p> <p>PD3006372</p>
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7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

<p><input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)</p>	<p><input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE</p>
<p><input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act</p>	<p><input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY</p>

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? YES NO

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:

<p>Department of Health and Human Services Food and Drug Administration CBER, HFM-99 1401 Rockville Pike Rockville, MD 20852-1448</p>	<p>Food and Drug Administration CDER, HFD-94 12420 Parklawn Drive, Room 3046 Rockville, MD 20852</p>	<p>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.</p>
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<p>SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE</p> <p><i>Doreen Frank</i></p>	<p>TITLE</p> <p><i>Director, Regulatory Affairs</i></p>	<p>DATE</p> <p><i>23 Jan 2006</i></p>
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9. USER FEE PAYMENT AMOUNT FOR THIS APPLICATION
\$383,700.00