

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-952**

**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

21-952

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 ® Liqui-Gels™ Capsules

ACTIVE INGREDIENT(S)

loratadine

STRENGTH(S)

10 mg

DOSAGE FORM

liquid filled capsules

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)

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*

*3/15/06*

**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

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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 # 21-952

SUPPL #

HFD # 560

Trade Name Claritin Liqui-Gels capsules

Generic Name loratadine 10 mg

Applicant Name Schering-Plough HealthCare Products

Approval Date, If Known June 16, 2008

### 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.

Applicant submitted a PK study comparing Claritin Liqui-Gels capsules 10 mg to Claritin 10 mg tablet

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?

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 10 mg tablets
NDA# 20-641	Claritin 1 mg/1 mL syrup
NDA# 20-704	Claritin 10 mg ODT Reditabs
NDA# 21-375	Alavert 10 mg ODT
NDA# 21-734	Loratadine 1 mg/1 mL syrup
NDA# 21-891	Children's Claritin 5 mg chewable tablet
NDA# 21-993	Claritin 5 mg ODT Reditabs

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:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

!

IND #

YES

!

! NO

! Explain:

Investigation #2

!

IND #

YES

!

! NO

! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES

Explain:

!

!

! NO

! Explain:

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: Elaine Abraham

Title: RPM

Date: 6/16/08

Name of Office/Division Director signing form: Joel Schiffenbauer

Title: Deputy Director, DNCE

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.**  
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/s/

-----  
Joel Schiffenbauer  
6/16/2008 06:47:05 AM

**PEDIATRIC PAGE**

**(Complete for all filed original applications and efficacy supplements)**

DA/BLA#: 21-952

Supplement Number: \_\_\_\_\_

NDA Supplement Type (e.g. SE5): \_\_\_\_\_

Division Name: DNCE

PDUFA Goal Date: 6/20/08

Stamp Date: \_\_\_\_\_

Proprietary Name: Claritin Liqui-Gels

Established/Generic Name: loratadine

Dosage Form: softgel capsule

Applicant/Sponsor: Schering-Plough

Indication(s) previously approved (please complete this question for supplements and Type 6 NDAs only):

- (1) \_\_\_\_\_
- (2) \_\_\_\_\_
- (3) \_\_\_\_\_
- (4) \_\_\_\_\_

**Q1:** Is this application in response to a PREA PMC?

Yes  Continue

No  Please proceed to Question 2.

If Yes, NDA/BLA#: \_\_\_\_\_

Supplement #: \_\_\_\_\_

PMC #: \_\_\_\_\_

Does the division agree that this is a complete response to the PMC?

Yes. **Skip to signature block.**

No. Please proceed to Question 2 and complete the Pediatric Page, as applicable.

**Q2:** Does this application provide for (If yes, please check all categories that apply and proceed to the next question):

(a) NEW  active ingredient(s);  indication(s);  dosage form;  dosing regimen; or  route of administration?\*

(b)  No. PREA does not apply. **Skip to signature block.**

**\* Note for CDER: SE5, SE6, and SE7 submissions may also trigger PREA.**

Pediatric use for each pediatric subpopulation must be addressed for each indication covered by current application under review. A Pediatric Page must be completed for each indication.

Number of indications for this pending application(s): 1

(Attach a completed Pediatric Page for each indication in current application.)

**Indication:** treatment of allergic rhinitis OTC

**Q3:** Does this indication have orphan designation?

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

No. Please proceed to the next question.

**Q4:** Is there a full waiver for all pediatric age groups for this indication (check one)?

Yes: (Complete Section A.)

No: Please check all that apply:

Partial Waiver for selected pediatric subpopulations (Complete Sections B)

Deferred for the remaining pediatric subpopulations (Complete Sections C)

Completed for some or all pediatric subpopulations (Complete Sections D)

Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)

Extrapolation in One or More Pediatric Age Groups (Complete Section F)

(Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

**IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL OR AT 301-796-0700.**

**Section A: Fully Waived Studies (for all pediatric age groups)**

Reason(s) for full waiver: (check, and attach a brief justification)

- Necessary studies would be impossible or highly impracticable because:
  - Disease/condition does not exist in children
  - Too few children with disease/condition to study
  - Other (e.g., patients geographically dispersed): \_\_\_\_\_
- 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.
- Evidence strongly suggests that product would be ineffective or unsafe in all pediatric subpopulations (Note: if studies are fully waived on this ground, this information must be included in the labeling.)

Justification attached.

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

**Section B: Partially Waived Studies (for selected pediatric subpopulations)**

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

			Reason (see below for further detail):				
	minimum	maximum	Not feasible <sup>#</sup>	Not meaningful therapeutic benefit <sup>*</sup>	Ineffective or unsafe <sup>†</sup>	Formulation failed <sup>A</sup>	
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input checked="" type="checkbox"/>	Other	0 yr. __ mo.	2 yr. __ mo.	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

Reason(s) for partial waiver (check reason corresponding to the category checked above, and attach a brief justification):

# Not feasible:

- Necessary studies would be impossible or highly impracticable because:
- Disease/condition does not exist in children
- Too few children with disease/condition to study
- Other (e.g., patients geographically dispersed): \_\_\_\_\_

For children less than 2 years of age, it is the Agency's decision not to label loratadine below this age based on the knowledge that children generally need to be exposed to allergens for at least two seasons before they develop a seasonal allergy. There is also concern that parents may not be able to properly diagnose allergic rhinitis condition in this age group in an OTC environment. There are other second-generation antihistamines (cetirizine) available by prescription and labeled down to the age of 6 months to treat (perennial) allergic rhinitis.

\* Not meaningful therapeutic benefit:

- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:

- Evidence strongly suggests that product would be ineffective or unsafe in this/these pediatric population(s) (Note: if studies are partially waived on this ground, this information must be included in the labeling.)

Δ Formulation failed:

- Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.)

Justification attached.

For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to Sections C and F and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Sections D and F and complete the PeRC Pediatric Assessment form); and/or (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Sections E and F). Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

**Section C: Deferred Studies (for remaining pediatric subpopulations). Complete Section F on Extrapolation.**

Check pediatric subpopulation for which pediatric studies are being deferred (and fill in applicable reason below):

Deferrals (for each or all age groups):				Reason for Deferral			Applicant Certification †	
				Ready for Approval in Adults	Need Additional Adult Safety or Efficacy Data	Other Appropriate Reason (specify below)*	Yes	No
Population	minimum	maximum						
<input type="checkbox"/> Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> All Pediatric Populations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Date studies are due (mm/dd/yy): _____								

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

\* Other Reason: \_\_\_\_\_

**IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL OR AT 301-796-0700.**

**Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and completed studies)**

*Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the target pediatric subpopulation needing studies. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as pharmacokinetic and safety studies.*

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:

Population	minimum	maximum	Extrapolated from:	
			Adult Studies?	Other Pediatric Studies?
<input type="checkbox"/> Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input checked="" type="checkbox"/> Other	2 yr. __ mo.	17 yr. __ mo.	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

*Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.*

*If there are additional indications, please complete the attachment for each one of those indications. Otherwise, this Pediatric Page is complete and should be signed and entered into DFS.*

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

(Revised: 4/2008)

**NOTE: If you have no other indications for this application, you may delete the attachments from this document.**

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/s/

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Elaine Abraham  
6/6/2008 08:27:02 AM

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.

20 Nov 2006

---

Date

APPEARS THIS WAY ON ORIGINAL

# CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

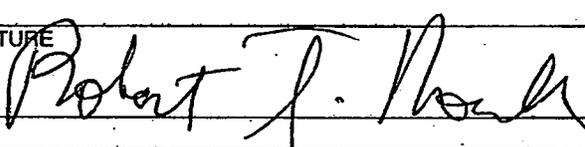
With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the 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. CL2004-02	
	/	/

- (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 Robert T. Nowak, Ph.D.	TITLE Director, Clinical and Claims Research
FIRM / ORGANIZATION Schering Plough HealthCare Products, Inc.	
SIGNATURE 	DATE 3/13/06

**Paperwork Reduction Act Statement**

This 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

b(4)

MEMORANDUM

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

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DATE: November 28, 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 21-952, Claritin®  
(Loratadine) Liquigel® Capsules 10 mg, 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 portion of the following bioequivalence study:

**Study CL2004-02:** A Single dose, Comparative, Randomized, Crossover Bioequivalence Study of Two Dosage Forms of Loratadine: 10 mg Claritin® Liqui-Gel® and 10 mg Claritin® Tablet

The analytical portion of this study was conducted at \_\_\_\_\_ DNCE did not request inspection of the clinical portion of the study. Following the inspection at \_\_\_\_\_ (10/23-27/06), Form FDA-483 was issued. Our evaluations 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 CL2004-02: Run 5ZMO-1-A and 9ZMO-1-A for loratadine (SCH 29851) and runs 15ZMO-2-A and 20ZMO-2-A for desloratadine (SCH 34117).

Since > 50% of the low QCs failed (i.e., > ±15% of the intended concentration) in the aforementioned analytical runs, the accuracy of the runs cannot be assured. The

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b(4)

firm's run acceptance criterion<sup>1</sup>, requiring only — QCs to pass at each level, is not adequate. 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:

b(4)

Analyte	Run	Subjects	Samples
Loratadine	5ZMO-1-A	13, 14, 15	553-575, 599-690
	9ZMO-1-A	25, 26, 27	1105-1242
Desloratadine	15ZMO-2-A	43, 44, 45	1933-2070
	20ZMO-2-A	2, 9, 11, 14, 15, 16, 17, 20, 21, 24, 26, 28, 30, 34, 39, 45	47,380,401,470,629-630,654-655,677-678,722,741-742,902-903,952-953,1086-1087,1157-1158,1264,1374-1375,1519,1542,1777-1778,1781,2058-2060

2. The sponsor did not establish 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.

b(4)

While the sponsor's procedures are of concern, less than 2% of the samples were re-assayed as PK repeats. The repeat and original results were included in Tables 9 and 10 of the final report. It should be noted that 76% of the repeat results were within 20% of the original value for Project ZMO. Although one C<sub>max</sub> sample was included for re-assay (Subject 24, Period II, 2.5 hr for desloratadine), the repeat result was within 1% of the original value.

**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:

<sup>1</sup> Schering Plough provided — the run acceptance criteria for the study.

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- Loratadine: Subjects 13, 14, 15, 25, 26 and 27
- Desloratadine: Subjects 43, 44, 45, 2 (Period I, 0 hr), 9 (Period I, 5.5 hr; Period II, 4.5 hr), 11 (Period I, 4.5 hr), 14 (Period II, 3.5 and 4 hrs), 15 (Period I, 4.5 and 5 hrs; Period II, 4.5 and 5 hrs), 16 (Period II, 4 hr), 17 (Period I, 2 and 2.5 hrs), 20 (Period II, 2 and 2.5 hrs), 21 (Period II, 4 and 4.5 hrs), 24 (Period II, 2 and 2.5 hrs), 26 (Period I, 3 and 3.5 hrs), 28 (Period I, 96 hr), 30 (Period II, 16 and 24 hrs), 34 (Period I, 0 hr; Period II, 0 hr), 39 (Period II, 2.5, 3 and 4.5 hrs), and 45 (Period II, 5, 5.5 and 6 hrs).

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

John A. Kadavil, Ph.D.

Final Classification: VAI \_\_\_\_\_

b(4)

CC:  
HFD-45/RF  
HFD-48/Himaya/Kadavil/CF  
DNCE/Patel/Abraham (via DFS)  
HFR-CE2545/Milazzo  
Draft: JAK 11/28/06  
Edit: MKY 11/28/06  
DSI: O:\BE\eircover\21952sch.lor.doc  
FACTS: 747834

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/s/

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John Kadavil

12/6/2006 01:06:31 PM

PHARMACOLOGIST

Paper copy signed by Dr. Viswanathan on 12/4/06 and  
available upon request.

## MEMORANDUM OF TELECON

DATE: October 19, 2006

APPLICATION NUMBER: NDA 21-952, Claritin

BETWEEN:

Name: Joyce Yates  
Bill Maclaughlin  
Phone: 888-560-9748  
Representing: Schering-Plough HealthCare Products

AND

Name: Shulin Ding, Ph.D.  
Gene Holbert, Ph.D.  
Linda D. Athey  
Division of Pre-Marketing Assessment II, Branch III

SUBJECT: Dissolution Method

BACKGROUND:

The applicant would like to use a dissolution method for stability batches using — at time point — minutes. b(4)

CALL:

The Teleconference was initiated at the request of the reviewing chemist, Gene Holbert, Ph.D., and concurrence of the Branch Chief. Dr. Holbert requested the applicant change the dissolution method specification to — at time point — minutes based on the data that they submitted. b(4)

The applicant stated that it sounds reasonable and they would submit an amendment changing the dissolution specification to — at time point — minutes. They will update the stability data in the amendment as well. b(4)

*{See appended electronic signature page}*

\_\_\_\_\_  
Linda D. Athey  
**Regulatory Health Project Manager for Quality**

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/s/

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Linda D Mullins-Athey  
10/19/2006 02:24:07 PM  
PROJECT MANAGER FOR QUALITY



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-952

INFORMATION REQUEST LETTER

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

Dear Ms. Frank:

Please refer to your August 2, 2005, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Claritin (Loratadine) Liqui-gel capsules 10mg.

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. Please submit dissolution data and profiles at 50 and 75 rpm for the biobatch and stability batches.
2. Submit updated stability data.

If you have any questions, call Linda Mullins Athey, Regulatory Health Project Manager for Quality, at 301-796-2096.

Sincerely,

*{See appended electronic signature page}*

Moo-Jhong Rhee, Ph.D.  
Chief, Branch III  
Pre-Marketing Assessment Division II  
Office of New Drug Quality Assessment  
Center for Drug Evaluation and Research

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/s/

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Moo-Jhong Rhee  
10/2/2006 10:15:50 AM  
Chief, Branch III

## RECORD OF TELEPHONE CONFERENCE

**Date:** July 18, 2006  
**Project Manager:** Elaine Abraham  
**Subject:** Discuss biopharmaceutical issue in the filing issues letter  
**NDA:** 21-952  
**Sponsor:** Schering-Plough HealthCare Products (SPHCP)  
**Product Name:** Claritin Liqui-Gel Capsules 10 mg  
**Phone No:** (888) 560-9748

**FDA participants:** Tayo Fadiran, Ph.D., Clinical Pharmacology Team Leader  
Shinja Kim, Ph.D., Clinical Pharmacology Reviewer  
Parthá Roy, Ph.D., Clinical Pharmacology Reviewer  
Elaine Abraham, RPM

**S-P participants:** John O'Mullane, Ph.D., Group Vice President, R & D  
Doreen Frank, Director, Regulatory Affairs  
Bill McLaughlin, Ph. D, Research Fellow, Pharmaceutical R & D  
Robert Nowak, Director, Clinical Research  
Nancy Pierro, Manager, Regulatory Affairs  
Joyce Yates, Director, Regulatory Affairs

Background: SPHCP submitted an NDA for Claritin Liqui-Gel Capsules 10 mg on March 15, 2006. In FDA's filing issues letter sent May 25, 2006, the lack of a study determining food effect for this formulation was noted as a potential review issue. As the food effect of Claritin has been well defined based on previous NDA approvals, an option was given for SPHCP to provide a comparative in vitro dissolution profile of the proposed formulation to the approved tablet formulation. SPHCP requested this teleconference on June 19, 2006, to gain a better understanding of FDA's request and to discuss the bioequivalence data submitted in the NDA. A meeting package was submitted on July 13, 2006.

**Note:** FDA informed SPHCP prior to the meeting that the second question would not be discussed. The second question involved a re-analysis of the bioequivalence data based on a DSI audit of the clinical site used for NDA 21-952. The re-analysis showed a 90% confidence interval for the ratio of loratadine Cmax was below 0.80. SPHCP asked if these data would support approval. FDA considers this a review issue that could not be addressed during the teleconference.

Question 1: *The Agency's Filing Communication letter dated May 25, 2006 requested SPHCP to submit the following information:*

- *Additional data to support that the food effect for this formulation is expected to be the same as that seen for the Claritin tablet, such as a comparative in vitro*

*dissolution profile of the proposed formulation to the approved tablet formulation.*

*SPHCP subsequent to filing the NDA conducted a Single Dose, Comparative, Randomized, Crossover Bioequivalence Study to Evaluate the Food Effect of Loratadine Soft Gelatin Capsules. The objective of this single-dose, two-way crossover study was to evaluate the relative bioavailability of 10 mg loratadine administered as one soft, gelatin capsule under fed and fasted conditions. A summary of the study is provided in Attachment 1. Based upon the results of this study and the well documented known food effect of loratadine summarized and presented in the marketing application in Module 2, Section 2.5.2. (Attachment 2), the food effect of Claritin Liqui-Gels is not clinically significant. Does the Agency agree that the data from the study presented in Attachment 1 supports the conclusion that the food effect of loratadine is not considered to effect clinical efficacy?*

Discussion: SPHCP stated that they conducted the food effect study after receiving FDA's filing issues letter. They noted that the food effect does not influence the effectiveness of the product, and asked if this study satisfies FDA. FDA responded that SPHCP should have discussed the design of the study with us prior to initiating the study. The proposed product (Claritin Liqui-gels) should have been compared to the approved product (Claritin tablets).

FDA stated that it would be difficult to evaluate the data from this study and that a cross study comparison would be needed. FDA asked why this particular design was chosen. SPHCP determined that a fed vs. fasted study was necessary. SPHCP maintained that the results were similar to those reported earlier. FDA responded that the results showed a doubling of the parent drug under fed conditions; while normally a 30 to 40% increase has been shown for other Claritin formulations.

SPHCP asked if FDA had a safety concern based on the increase under fed conditions. FDA responded that the food effect is very different from the tablet and noted that this would be a review issue for the medical officer. SPHCP believed that in vitro dissolution and pharmacokinetics of the proposed product are similar to those of Claritin tablet. FDA responded that evaluating similarities would be a review issue.

FDA stated that this is not a stand alone 505(b)(1) application because it is based on the safety and efficacy of Claritin tablet.

SPHCP asked if the review of the re-analysis of data for NDA 21-891, Children's Claritin chewable tablets, had been completed. FDA responded that this NDA is still under review.

**Abraham, Elaine G**

---

**From:** Frank, Doreen [doreen.frank@spcorp.com]  
**Sent:** Monday, June 19, 2006 12:10 PM  
**To:** Abraham, Elaine G  
**Subject:** Teleconference Request - NDA 21-952

Dear Elaine,

Reference is made to our May 31, 2006 filing communication letter (74-day letter) for Claritin Liqui-Gel capsules, 10 mg. The Agency requested additional data to support that the food effect for this formulation is expected to be the same as that seen for the Claritin tablet. Schering-Plough HealthCare Products (SPHCP) is requesting a teleconference with the Biopharm reviewer to discuss the food effect comment as well as the bioequivalence data submitted in support of the application. I would greatly appreciate your assistance in scheduling the meeting.

Proposed meeting attendees from SPHCP:  
Doreen Frank, Director Regulatory Affairs  
Robert Nowak, Director Clinical Research  
Nancy Pierro, Manager Regulatory Affairs

Thank you in advance,  
Doreen Frank  
Director, Regulatory Affairs  
doreen.frank@spcorp.com  
(908) 473-1655  
(908) 473-1741 (fax)

APPEARS THIS WAY ON ORIGINAL

8/17/2006

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/s/

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Elaine Abraham  
8/17/2006 10:37:06 AM  
CSO

H. Abraham

MEMORANDUM

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

DATE: June 26, 2006

TO: Director, Investigations Branch  
6000 Metro Drive, Suite 101  
Baltimore, MD 21215

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

SUBJECT: FY 2006, High Priority CDER User Fee NDA, Pre-Approval  
Data Validation Inspection, Bioresearch monitoring,  
Human Drugs, CP 7348.001

RE: NDA 21-952  
DRUG: Claritin (Loratadine) Liqui-gel Capsules 10  
mg  
SPONSOR: Schering Plough

This memo requests that you arrange an inspection of the analytical portion of the following pivotal bioequivalence study. The inspection is related to high priority CDER user fee NDA. The Agency relies on these pivotal BE studies for the approval of this application; these BE study is the only clinical trial conducted for the NDA 21-952. A DSI scientist with specialized knowledge in the evaluation of bioanalytical methods will participate in the inspection to provide scientific and technical expertise. Due to review division deadlines, the inspections should be completed prior to September 29, 2006.

Study # CL2004-02: A Single dose, Comparative, Randomized, Crossover Bioequivalence Study of Two Dosage Forms of Loratadine: 10 mg Claritin Liqui-gel and 10 mg Claritin Tablet

Analytical Site: \_\_\_\_\_

b(4)

Analytical Investigator: \_\_\_\_\_

Page 2 - BIMO Assignment, NDA 21-952, Claritin (Loratidine)  
Liqui-gel Capsules, 10 mg

Instrumentation: LC/MS/MS

— analyzed plasma samples from Study CL2004-02 for concentrations of SCH 29851 (Loratidine) and its metabolite SCH 34117 (Desloratidine).

b(4)

All pertinent items related to the analytical method should be examined and the sponsor's data should be audited. The chromatograms provided in the NDA submission should be compared with the original documents at the firm. The actual assay of the subject plasma samples, as well as the variability between and within runs, QC, the number of repeat assays of the subject plasma samples, and the reason for such repetitions, if any, should be examined. In addition to the standard investigation involving the source documents, the files of communication between the analytical site and the sponsor should be examined for their content.

Following the identification of the investigators, background material will be forwarded directly. **A members from the GLP and Bioequivalence Team in DSI will participate in the inspection at**

b(4)

Headquarters Contact Person: Jagan Mohan R. Parepally, Ph.D.  
(301) 594-2042

cc:

DSI/RF

DSI/GLPBB/Parepally/Himaya/CF

OCP/DCP2/Kim (NDA 21-952)

DNCE/Abraham (WO22, RM5410)

HFR-CE250/Salisbury (BIMO Monitor; please fax)

Draft: JP 06/26/06

Edit: MKY 06/27/06

DSI 5702; O:\BE\assigns\bio21952.doc

FACTS 747834

FEL: \_\_\_\_\_

b(4)



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

**FILING COMMUNICATION**

NDA 21-952

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

Dear Ms. Frank:

Please refer to your August 2, 2005 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Claritin (loratadine) Liqui-gel capsules 10 mg.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on May 15, 2006, in accordance with 21 CFR 314.101(a).

In our filing review, we have identified the following potential review issues:

1. Your NDA submission did not include a food effect study on Claritin Liqui-gel capsules.
2. Labeling was not submitted in electronic format.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

We request that you submit the following information:

1. Additional data to support that the food effect for this formulation is expected to be the same as that seen for the Claritin tablet, such as a comparative *in vitro* dissolution profile of the proposed formulation to the approved tablet formulation.
2. Labeling in electronic format.

Please respond only to the above requests for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

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/s/

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Leah Christl  
5/25/2006 09:01:28 AM

**DSI CONSULT**

**Request for Biopharmaceutical Inspections**

**DATE:** May 18, 2006

**TO:** Associate Director for Bioequivalence  
Division of Scientific Investigations, HFD-48

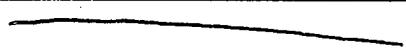
**THROUGH:** Andrea Leonard Segal, M.D.  
Director, Division of Nonprescription Clinical Evaluation (DNCE)

**FROM:** Elaine Abraham, Regulatory Project Manager, DNCE

**SUBJECT:** Request for Biopharmaceutical Inspections  
NDA 21-952  
Claritin (loratadine) liqui-gel capsules 10 mg

**Study/Site Identification:**

As discussed with you, the following studies/sites pivotal to approval have been identified for inspection:

Study #	Analytical Site (name, address, phone, fax, contact person, if available)
CL2004-02	

b(4)

**Goal Date for Completion:**

We request that the inspections be conducted and the Inspection Summary Results be provided by **October 16, 2006**. We intend to issue an action letter on this application by **January 16, 2007**.

Should you require any additional information, please contact Elaine Abraham at (301) 796-0843.

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/s/

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Elaine Abraham  
5/22/2006 06:43:49 AM

Andrea Segal  
5/22/2006 07:58:52 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service  
Food and Drug Administration  
Rockville, MD 20857

NDA 21-952

**NDA ACKNOWLEDGMENT**

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

Dear Ms. Williams:

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 (loratadine) Liqui-gel capsules 10 mg

Review Priority Classification: Standard (S)

Date of Application: March 15, 2006

Date of Receipt: March 16, 2006

Our Reference Number: NDA 21-952

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 May 15, 2006, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be January 16, 2007.

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 21-952

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 Elaine Abraham, Regulatory Project Manager, at (301) 796-0843.

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/

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Leah Christl

5/5/2006 01:51:47 PM

**CONSULTATION RESPONSE**  
**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT**  
**OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY**  
**(DMETS; WO 22, MAIL STOP 4447)**

**DATE RECEIVED:**

April 19, 2006

**DESIRED COMPLETION DATE:**

October 15, 2006

**OSE REVIEW #:** 06-0117

**DATE OF DOCUMENT:**

March 15, 2006

**PDUFA DATE:**

January 16, 2007

**TO:** Andrea Leonard-Segal, MD  
Director, Division of Nonprescription Clinical Evaluation  
HFD-560

**THROUGH:** Alina Mahmud, R.Ph., M.S., Team Leader  
Denise Toyer, Pharm.D., Deputy Director  
Carol Holquist, R.Ph., Director  
Division of Medication Errors and Technical Support

**FROM:** Kimberly Pedersen, R.Ph., Safety Evaluator  
Division of Medication Errors and Technical Support

**PRODUCT NAME:**

**Claritin®**  
(Loratadine Capsules)  
10 mg

**SPONSOR:** Schering-Plough HealthCare Products, Inc.

**NDA#:** 21-952

**RECOMMENDATIONS:**

1. DMETS has no objections to the use of the "Liqui-gels™" descriptor in conjunction with the Claritin® proprietary name. This is considered a final decision. However, if approval of this application is delayed beyond 90 days from the signature date of this document, the name must be re-evaluated. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary and established names from the signature date of this document.
2. DMETS recommends implementation of the label revisions outlined in section III to minimize potential errors with the use of this product.
3. DDMAC does not provide comments on the promotional aspects of over-the-counter products. The Federal Trade Commission regulates the advertising of these products.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Diane Smith, Project Manager, at 301-796-0538.

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>

1. APPLICANT'S NAME AND ADDRESS

SCHERING PLOUGH HEALTHCARE PRODUCTS INC  
Doreen Frank  
Schering-Plough HealthCare Products 556 Morris Avenue  
Summit NJ 07901-1330  
US

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

21-952

2. TELEPHONE NUMBER

908-473-1655

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?

YES  NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW:

THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION

THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

NDA 19-658

3. PRODUCT NAME

Claritin Liqul-Gels Capsulés ( loratadine 10 mg capsules )

6. USER FEE I.D. NUMBER

PD3006446

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

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

A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE

THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act

THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY

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:

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

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

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

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE

*Doreen Frank*

TITLE

*Director, Reg Affairs*

DATE

*03/1/2006*

9. USER FEE PAYMENT AMOUNT FOR THIS APPLICATION

\$383,700.00

Form FDA 3397 (12/03)

**NDA REGULATORY FILING REVIEW**  
**(Including Memo of Filing Meeting)**

NDA # 21-952

Supplement #

Efficacy Supplement Type SE-

Trade Name: Claritin Liqui-gel Capsules

Established Name: loratadine

Strengths: 10 mg

Applicant: Schering-Plough HealthCare Products

Agent for Applicant:

Date of Application: March 15, 2006

Date of Receipt: March 16, 2006

Date clock started after UN:

Date of Filing Meeting: April 26, 2006

Filing Date: May 15, 2006

Action Goal Date (optional): November 16, 2006

User Fee Goal Date: January 16, 2007

Indication(s) requested: Relief of symptoms related 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:**

(0) 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.

(0) 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.) 3  
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: Schering-Plough has pediatric exclusivity for several of its NDAs
- 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: I 63,803
- End-of-Phase 2 Meeting(s) Date(s) \_\_\_\_\_ NO   
If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s) Date(s) \_\_\_\_\_ 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

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ATTACHMENT

**MEMO OF FILING MEETING**

DATE: April 26, 2006

**BACKGROUND:** NDA 21-952, Claritin Liqui-gel Capsules, an immediate release, liquid-filled capsule is a new dosage form that contains 10 mg loratadine. The product is intended for adults and children 6 years of age and over with a dose of one 10 mg capsule every 24 hours. A pediatric waiver is requested for children less than 6 years of age. Previously approved NDAs for Claritin include NDA 19-658 (Claritin tablet, 10 mg), NDA 20-641 (Children's Claritin Syrup, 5mg/5mL) and NDA 20-704 (Claritin Reditabs, 10mg). This NDA is referencing NDAs 19-658, 21-891, and 21-993 for pre-clinical and clinical information, foreign marketing history, and the safety update. A single-dose comparative, randomized, crossover bioequivalence study of two 5 mg Claritin Chewable tablets (test product) to one 10 mg Claritin tablet (reference product) was conducted for this NDA. The issues identified in the filing meeting were the lack of a food effect study. Because Claritin is well characterized by previous NDAs, we will request additional data to support that the food effect for this formulation is expected to be the same as that seen for Claritin tablet, such as a comparative in vitro dissolution profile of the proposed formulation to the approved tablet formulation. (Provide a brief background of the drug, e.g., it is already approved and this NDA is for an extended-release formulation; whether another Division is involved; foreign marketing history; etc.)

**ATTENDEES:** Andrea Leonard-Segal, Daiva Shetty, Marina Chang, Shulin Ding, Emmanuel Fadiran, Ching-Long (Joe) Sun in addition to reviewers below.

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

<u>Discipline</u>	<u>Reviewer</u>
Medical:	Lolita Lopez
Secondary Medical:	
Statistical:	
Pharmacology:	Lawrence Sancilio
Statistical Pharmacology:	
Chemistry:	Gene Holbert
Environmental Assessment (if needed):	
Biopharmaceutical:	Shinja Kim
Microbiology, sterility:	
Microbiology, clinical (for antimicrobial products only):	
DSI:	Martin Yau, Jagan Parepally
Regulatory Project Management:	Elaine Abraham
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  FILE  REFUSE TO FILE

STATISTICS N/A  FILE  REFUSE TO FILE

BIOPHARMACEUTICS FILE  REFUSE TO FILE

- 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): data to support that the food effect for this formulation is expected to be the same as that seen for Claritin tablet, such as a comparative in vitro dissolution profile of the proposed formulation to the approved tablet formulation.

**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.

Elaine Abraham  
Regulatory Project Manager, HFD-560

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## Appendix A to NDA Regulatory Filing Review

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

- (0) it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)
- (0) 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)
- (0) 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.)
- (0) 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).

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**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, YES  NO   
ORP?

*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

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

YES  NO

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

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Elaine Abraham  
11/15/2006 08:48:20 AM  
CSO

## ACTION PACKAGE CHECKLIST

Application Information		
BLA # NDA # 21-952	BLA STN# NDA Supplement #	If NDA, Efficacy Supplement Type
Proprietary Name: Claritin Liqui-gels Established Name: loratadine 10 mg Dosage Form: capsules		Applicant: Schering-Plough HealthCare Products
RPM: Elaine Abraham		Division: DNCE      Phone # (301) 796-0843
<p>NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1)    <input type="checkbox"/> 505(b)(2)</p> <p>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><b>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.</b></p> <p><input type="checkbox"/> Confirmed      <input type="checkbox"/> Corrected</p> <p>Date:</p>
❖ User Fee Goal Date		6/20/08
❖ Action Goal Date (if different)		6/20/08
❖ 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 (specify type and date for each action taken)		<input type="checkbox"/> None AE 1/12/07
❖ Advertising (approvals only) Note: If accelerated approval (21 CFR 314.510/601.41), advertising must have been submitted and reviewed (indicate dates of reviews)		<input type="checkbox"/> Requested in AP letter <input type="checkbox"/> Received and reviewed

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❖ Application Characteristics	
Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): 3	
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"> <li>Applicant is on the AIP</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>This application is on the AIP                             <ul style="list-style-type: none"> <li>Exception for review (<i>file Center Director's memo in Administrative Documents section</i>)</li> <li>OC clearance for approval (<i>file communication in Administrative Documents section</i>)</li> </ul> </li> </ul>	<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"> <li>Office of Executive Programs (OEP) liaison has been notified of action</li> </ul>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> <li>Press Office notified of action</li> </ul>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> <li>Indicate what types (if any) of information dissemination are anticipated</li> </ul>	<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>	
<b>Summary Reviews</b>	
❖ Summary Reviews (e.g., Office Director, Division Director) (indicate date for each review)	1/12/07, 6/16/08
❖ BLA approvals only: Licensing Action Recommendation Memo (LARM) (indicate date)	
<b>Labeling</b>	
❖ Package Insert	
<ul style="list-style-type: none"> <li>• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)</li> </ul>	
<ul style="list-style-type: none"> <li>• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)</li> </ul>	
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> <li>• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable</li> </ul>	
❖ Patient Package Insert	
<ul style="list-style-type: none"> <li>• Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling)</li> </ul>	
<ul style="list-style-type: none"> <li>• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)</li> </ul>	
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> <li>• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable</li> </ul>	
❖ Medication Guide	
<ul style="list-style-type: none"> <li>• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)</li> </ul>	
<ul style="list-style-type: none"> <li>• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)</li> </ul>	
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> <li>• Other relevant labeling (e.g., most recent 3 in class, class labeling)</li> </ul>	
❖ Labels (full color carton and immediate-container labels)	
<ul style="list-style-type: none"> <li>• Most-recent division-proposed labels (only if generated after latest applicant submission)</li> </ul>	
<ul style="list-style-type: none"> <li>• Most recent applicant-proposed labeling</li> </ul>	12/19/07, 4/14/08
❖ Labeling reviews and minutes of any labeling meetings (indicate dates of reviews and meetings)	<input checked="" type="checkbox"/> DMETS 11/17/06 <input type="checkbox"/> DSRCS <input type="checkbox"/> DDMAC <input type="checkbox"/> SEALD <input checked="" type="checkbox"/> Other reviews 8/16/06, 11/9/06, 4/28/08 <input type="checkbox"/> Memos of Mtgs

Administrative Documents	
❖ Administrative Reviews (RPM Filing Review/Memo of Filing Meeting; ADRA) ( <i>indicate date of each review</i> )	11/15/06
❖ 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"> <li>Center Director's Exception for Review memo</li> <li>If AP: OC clearance for approval</li> </ul>	
❖ 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"> <li>Outgoing Agency request for post-marketing commitments (<i>if located elsewhere in package, state where located</i>)</li> <li>Incoming submission documenting commitment</li> </ul>	<input checked="" type="checkbox"/> None
❖ Outgoing correspondence (letters including previous action letters, emails, faxes, telecons)	5/25/06, 7/18/06, 10/2/06, 10/19/06, 11/13/06, 1/12/07, 2/2/07
❖ Internal memoranda, telecons, email, etc.	
❖ Minutes of Meetings <ul style="list-style-type: none"> <li>Pre-Approval Safety Conference (<i>indicate date; approvals only</i>)</li> <li>Pre-NDA/BLA meeting (<i>indicate date</i>)</li> <li>EOP2 meeting (<i>indicate date</i>)</li> <li>Other (e.g., EOP2a, CMC pilot programs)</li> </ul>	<input type="checkbox"/> No mtg <input type="checkbox"/> No mtg 11/30/06, 12/15/06
❖ Advisory Committee Meeting <ul style="list-style-type: none"> <li>Date of Meeting</li> <li>48-hour alert or minutes, if available</li> </ul>	<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> )	11/29/06
❖ 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"> <li><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>)</li> <li><input type="checkbox"/> Review &amp; FONSI (<i>indicate date of review</i>)</li> <li><input type="checkbox"/> Review &amp; Environmental Impact Statement (<i>indicate date of each review</i>)</li> </ul>	11/29/06
❖ NDAs: Microbiology reviews (sterility & apyrogenicity) ( <i>indicate date of each review</i> )	<input checked="" type="checkbox"/> Not a parenteral product
❖ Facilities Review/Inspection <ul style="list-style-type: none"> <li>NDAs: Facilities inspections (include EER printout)</li> </ul>	Date completed: 10/5/06 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation

❖ BLAs: Facility-Related Documents <ul style="list-style-type: none"> <li>• Facility review (<i>indicate date(s)</i>)</li> <li>• Compliance Status Check (approvals only, both original and supplemental applications) (<i>indicate date completed, must be within 60 days prior to AP</i>)</li> </ul>	<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
<b>Nonclinical Information</b>	
❖ Pharm/tox review(s), including referenced IND reviews ( <i>indicate date for each review</i> )	9/19/06
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer ( <i>indicate date for each review</i> )	<input checked="" 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 type="checkbox"/> None requested
<b>Clinical Information</b>	
❖ Clinical review(s) ( <i>indicate date for each review</i> )	12/11/06, 5/12/08
❖ Financial Disclosure reviews(s) or location/date if addressed in another review	12/11/06
❖ 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> )	5/12/08
❖ Risk Management Plan review(s) (including those by OSE) ( <i>indicate location/date if incorporated into another review</i> )	
❖ 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	
• Clin Pharm Studies	12/6/06
❖ Statistical Review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None
❖ Clinical Pharmacology review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None      11/30/06, 1/26/07, 4/25/08

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## 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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this page is the manifestation of the electronic signature.**  
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/s/

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Elaine Abraham ✖  
6/26/2008 07:23:02 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-952

Schering-Plough HealthCare Products.  
Attention: Nancy Pierro  
Associate Director, Regulatory Affairs  
556 Morris Avenue  
Summit, NJ 07901-1330

Dear Ms. Pierro:

Please refer to your submission dated March 15, 2006, requesting a waiver for pediatric studies for Claritin (loratadine) Liqui-gel Capsules 10 mg.

We have reviewed the submission and agree that a waiver is justified for pediatric studies in patients under 2 years of age for Claritin Liqui-gel Capsules 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. The reason for granting the waiver is that 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 pediatric patients above the age of 2 years.

If you have questions, contact Elaine Abraham, Regulatory Project Manager, at (301) 796-0843.

Sincerely,

*{See appended electronic signature page}*

Joel Schiffenbauer, M.D.  
Deputy Director  
Division of Nonprescription Clinical Evaluation  
Office of Nonprescription Products  
Center for Drug Evaluation and Research

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

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Joel Schiffenbauer  
2/2/2007 11:27:05 AM

**MEMORANDUM OF MEETING MINUTES**

**MEETING DATE:** November 30, 2006  
**TIME:** 10:30 - 11:00 a.m.  
**LOCATION:** Teleconference

**APPLICATION:** NDA 21-952  
**SPONSOR:** Schering-Plough HealthCare Products, Inc.  
**DRUG NAME:** Claritin (loratadine 10 mg) Liqui-gel Capsules  
**TYPE OF MEETING:** Type C - Labeling discussion  
**IMTS#:** 20705

**MEETING CHAIR:** Andrea Leonard-Segal, M.D.

**MEETING RECORDER:** Elaine Abraham, R.Ph.

**FDA ATTENDEES:**

Division of Nonprescription Clinical Evaluation

Andrea Leonard-Segal, M.D.	Director
Daiva Shetty, M.D.	Medical Team Leader
Bindi Nikhar, M.D.	Medical Team Leader
Lolita Lopez, M.D.	Medical Officer
Elaine Abraham, R.Ph.	Regulatory Project Manager
Leah Christl, Ph.D.	Chief, Project Management Staff

Division of Nonprescription Regulation Development

Marina Chang, R.Ph.	Team Leader
Cazemiro Martin	Regulatory Review Chemist

Office of Clinical Pharmacology

Emmanuel Fadiran, Ph.D.	Clinical Pharmacology Team Leader
Shinja Kim, Ph.D.	Clinical Pharmacology Reviewer

**EXTERNAL CONSTITUENT ATTENDEES:**

Schering-Plough HealthCare Products

Dr. Luis Salmun	Sr. Director, Medical Affairs
Robert Nowak, Ph.D.	Director, Clinical Research
Joyce Yates	Director, Regulatory Affairs

**BACKGROUND:**

FDA faxed labeling comments to Schering-Plough HealthCare Products (SPHCP) on November 13, 2006 for NDA 21-952 Claritin Liqui-gel (loratadine 10 mg) Capsules. FDA requested that that SPHCP revise the labeling for the 10- and 30-count cartons as follows:

1. Delete the phrase \_\_\_\_\_ wherever it appears in the labeling of this product, unless there are data to support this claim. The data must be reviewed by the agency before the claim can be made in the labeling. b(4)
2. Revise the Directions section of the "Drug Facts" labeling to include the following bulleted statement: "• **take on an empty stomach. Taking with food may cause drowsiness.**" This statement must appear as the first bulleted statement in bold type under this heading. Based on the food effect study that you submitted, this drug product showed greater bioavailability when taken with food. As the data indicated in the application, the administration of Claritin Liqui-Gels Capsules (loratadine 10 mg) with food increased the loratadine Cmax (53.06%), AUC0-t (121.13%), and AUC0-∞ (118.03%). Consequently, drowsiness may occur if this product is taken with food. Consumers should be alerted to this possible effect.

SPHCP submitted a meeting request on November 20, 2006 to discuss these labeling issues. SPHCP submitted a meeting package on November 28, 2006.

**MEETING OBJECTIVE:**

To reach agreement on the proposed labeling with regard to the two comments faxed by FDA.

**DISCUSSION:**

Following introductions and a brief discussion of the purpose of the meeting, the discussion opened with the first labeling issue: FDA's recommendation that \_\_\_\_\_ language be deleted from the labeling. SPHCP stated that the liquid-gel capsules are a popular dosage form because they are generally understood in the industry to be : \_\_\_\_\_ terminology is seen frequently in the marketplace on monograph products and dietary supplements. b(4)

FDA responded that this terminology is considered promotional and there are no data to support this claim. FDA pointed out that monograph products and dietary supplements follow different regulatory pathways from new drug applications. Also, information on the principal display panel (PDP) should be data-driven.

In their meeting package, SPHCP requested that they retain the \_\_\_\_\_ labeling claim but agree to generate confirmatory data as a Phase IV commitment. SPHCP asked if this option would be acceptable to FDA. FDA responded that they would not be amenable to a Phase IV commitment, but SPHCP could always propose a labeling change after action is taken on the NDA. FDA stated that they felt it would be difficult to interpret the data from any study conducted in support this claim.

b(4)

SPHCP asked if FDA is familiar with Imodium Liqui-gels, a product marketed under an NDA which has an \_\_\_\_\_ claim. FDA stated that if labeling with \_\_\_\_\_ language was approved, that is was done in error and that they would look into correcting the label. SPHCP agreed to remove \_\_\_\_\_ language from the labeling at this time.

b(4)

Regarding the statement that FDA recommended be added to the labeling related to food effect, SPHCP briefly summarized the information contained in the meeting package. SPHCP stated that there is an increased AUC and Cmax for liqui-gels administered with food vs. fasted conditions, but levels under fed conditions are similar to other approved loratadine 10 mg formulations. SPHCP pointed out their cross-study comparison contained in the meeting package. FDA responded that cross-study comparisons are problematic and difficult to assess. For example, the fasted mean AUC for loratadine from the bioequivalence Study 2004-02 is about 40% greater than the fasted mean AUC from the food effect Study CL2005-17. The evidence is strong that there is a food effect. SPHCP would have to show that the liqui-gels are similar to Claritin 10 mg tablets in a food effect bioequivalence study.

SPHCP questioned whether the levels with food are high enough to cause drowsiness. FDA responded that this is a possibility and would be dependent on the individual because the results for loratadine are highly variable. FDA pointed out patient # 12 who had three times more systemic exposure (AUC) under fed conditions compared to that under fasted conditions.

SPHCP pointed out non-drowsy language on the PDP of Claritin products, and noted that they find any statements about taking with food to avoid drowsiness to be troublesome. SPHCP proposed changing the language to simply adding "take on an empty stomach" in the directions. FDA responded that "take on an empty stomach" alone is not sufficient. It is not informative enough to the consumer because unexpected drowsiness could be a safety issue. FDA pointed out that OTC antihistamines with the potential to cause drowsiness have this warning on their product labels. SPHCP asked about conducting a bioequivalence study comparing the liquid-gels to Claritin tablets under fed conditions, and FDA agreed that this would be acceptable.

#### AGREEMENTS AND ACTION ITEMS:

1. SPHCP agreed to remove \_\_\_\_\_ language from the labeling.
2. SPHCP agreed to add language recommended by FDA related to food effect in the directions.
3. SPHCP agreed to submit revised labeling based on the FDA's comments.

b(4)

4. In order to support removing any food effect language from the labeling, SPHCP would need to conduct a food effect bioequivalence study comparing the liqui-gel formulation to Claritin tablets 10 mg.

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/s/

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Andrea Segal

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