

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-150/S007

**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

21-150 Rx-to-OTC Supp.

NAME OF APPLICANT/ NDA-HOLDER

Pfizer Inc.

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)

ZYRTEC-D 12 HOUR

ACTIVE INGREDIENT(S)

cetirizine HCl

pseudoephedrine HCl

STRENGTH(S)

5 mg

120 mg

DOSAGE FORM

Tablet, extended release

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.

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 4525358	b. Issue Date of Patent 6/25/1985	c. Expiration Date of Patent 6/25/2007
d. Name of Patent Owner UCB Inc. Legal Department	Address (of Patent Owner) 1950 Lake Park Drive	
	City/State Smyrna, GA	
	ZIP Code 30080	FAX Number (if available)
	Telephone Number (770) 970-7500	E-Mail Address (if available)
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)	Address (of agent or representative named in 1.e.)	
	City/State	
	ZIP Code	FAX Number (if available)
	Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		
<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No		
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?		
<input type="checkbox"/> Yes <input checked="" type="checkbox"/> 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

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) 23-31 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.) The "Indications and Usage" section of the proposed labeling describes seasonal and perennial allergic rhinitis symptoms which indications are covered by the cited claims that encompass achieving an antiallergic (claim 23) or antihistaminic (claims 23-27) effect and treating allergic symptoms (claims 28-31) by administration of the product for which approval is sought.

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 a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in 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

Bruce A. Pokras

11/27/2006

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

Check applicable box and provide information below.

<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Bruce A. Pokras	
Address 201 Tabor Road	City/State Morris Plains, NJ
ZIP Code 07950	Telephone Number (973) 385-5399
FAX Number (if available) (973) 385-7330	E-Mail Address (if available) bruce.a.pokras@pfizer.com

The public reporting burden for this collection of information has been estimated to average 9 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send

comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

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CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

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ZYRTEC-D 12 HOUR

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120 mg

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1. GENERAL

a. United States Patent Number

6489329

b. Issue Date of Patent

12/3/2002

c. Expiration Date of Patent

4/8/2016

d. Name of Patent Owner

UCB S.A.

Address (of Patent Owner)

Allée de la Recherche, 60

City/State

1070 Brussels

ZIP Code

Belgium

FAX Number (if available)

Telephone Number

+32/2/559.99.99

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)

UCB Inc.

Legal Department

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

1950 Lake Park Drive

City/State

Smyrna, GA

ZIP Code

30080

FAX Number (if available)

Telephone Number

(770) 970-7500

E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

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

2. Drug Substance (Active Ingredient)

- 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
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- 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

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 a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in manufacture, use, or sale of the drug product. Yes

6. Declaration Certification

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Date Signed

Bruce A. Pokras

11/27/2006

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Check applicable box and provide information below.

<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Bruce A. Pokras	
Address 201 Tabor Road	City/State Morris Plains, NJ
ZIP Code 07950	Telephone Number (973) 385-5399
FAX Number (if available) (973) 385-7330	E-Mail Address (if available) bruce.a.pokras@pfizer.com

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5 mg

120 mg

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1. GENERAL

a. United States Patent Number

6469009

b. Issue Date of Patent

10/22/2002

c. Expiration Date of Patent

7/13/2019

d. Name of Patent Owner

UCB S.A.

Address (of Patent Owner)

Allée de la Recherche, 60

City/State

1070 Brussels

ZIP Code

Belgium

FAX Number (if available)

Telephone Number

+31/2/559.99.99

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)

UCB Inc.
Legal Department

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

1950 Lake Park Drive

City/State

Smyrna, GA

ZIP Code

30080

FAX Number (if available)

Telephone Number

(770) 970-7500

E-Mail Address (if available)

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

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) 9-11 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.) The "Indications and Usage" section of the proposed labeling describes seasonal and perennial allergic rhinitis symptoms which indications are covered by the cited claims that encompass treating rhinitis by administration of the product for which approval is sought.

5. No Relevant Patents

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Date Signed

Bruce A. Pokras

11/27/2004

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<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Bruce A. Pokras	
Address 201 Tabor Road	City/State Morris Plains, NJ
ZIP Code 07950	Telephone Number (973) 385-5399
FAX Number (if available) (973) 385-7330	E-Mail Address (if available) bruce.a.pokras@pfizer.com

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a. United States Patent Number

7014867

b. Issue Date of Patent

3/21/2006

c. Expiration Date of Patent

6/10/2022

d. Name of Patent Owner

UCB Farchim SA

Address (of Patent Owner)

Chemin de Croix Blanche, 10

City/State

CH-1630 Bulle

ZIP Code

Switzerland

FAX Number (if available)

Telephone Number

+41/26/919-0200

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)

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30080

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Telephone Number

(770) 970-7500

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- 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

Bruce A. Pokras

11/27/2006

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

Check applicable box and provide information below.

<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Bruce A. Pokras	
Address 201 Tabor Road	City/State Morris Plains, NJ
ZIP Code 07950	Telephone Number (973) 385-5399
FAX Number (if available) (973) 385-7330	E-Mail Address (if available) bruce.a.pokras@pfizer.com

The public reporting burden for this collection of information has been estimated to average 9 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send

comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

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

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

EXCLUSIVITY SUMMARY

NDA # 21-150

SUPPL # 007

HFD # 560

Trade Name Zyrtec-D

Generic Name cetirizine HCl 5 mg/pseudoephedrine HCl 120 mg

Applicant Name McNeil (agent for Pfizer)

Approval Date, If Known November 9, 2007

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

SE6

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

YES

NO

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

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

d) Did the applicant request exclusivity?

YES NO

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

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

YES NO

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

No

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

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

YES NO

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

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES NO

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

NDA#

NDA#

NDA#

2. Combination product.

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

YES NO

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

NDA#

NDA#

NDA#

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

IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

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

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

YES NO

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

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

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

YES NO

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

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

YES NO

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

YES NO

If yes, explain:

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

YES NO

If yes, explain:

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

Studies in-house from the original application, NDA 21-150 were re-reviewed for this efficacy supplement

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:

Investigations A3771001, A3771002, A3771007 from the original Rx NDA, 21-150

- 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"):

none

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 ! NO
Explain: ! 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: 11/16/07

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

Title: Director, DNCE

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

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

/s/

Andrea Segal

11/16/2007 12:40:37 PM

20.0 OTHER

20.1 Pediatric Assessment

Pediatric Use Information: Request for full waiver

As required under 21 CFR 314.55, we herewith request a full waiver for submission of pediatric use information because Zyrtec-D 12 Hour Tablets is not likely to be used in a substantial number of pediatric patients.

Zyrtec-D 12 Hour (cetirizine HCl/pseudoephedrine HCl; NDA 21-150) Tablets were approved on August 10, 2001 for the relief of nasal and non-nasal symptoms associated with seasonal or perennial allergic rhinitis in adults and children 12 years of age and older. The extended-release dose of pseudoephedrine HCl in this product (120 mg) exceeds that approved for use in children under 12 years of age. Zyrtec-D 12 Hour was not studied in the pediatric population since it was not likely to be used in pediatric patients.

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PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA #: 21-150 Supplement Type (e.g. SE5): SE6 Supplement Number: 007

Stamp Date: January 11, 2007 PDUFA Goal Date: November 11, 2007

HFD ONP/DNCE Trade and generic names/dosage form: Zyrtec-D (cetirizine HCl 5 mg/ pseudoephedrine HCl 120 mg) tablets

Applicant: McNeil (Agent for Pfizer) Therapeutic Class: Antihistamine/decongestant

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

- Yes. Please proceed to the next question.
 No. PREA does not apply. Skip to signature block.

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

Indication(s) previously approved (please complete this section for supplements only): _____

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

Number of indications for this application(s): _____

Indication #1: _____

Is this an orphan indication?

- Yes. PREA does not apply. Skip to signature block.
 No. Please proceed to the next question.

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

- Yes: Please proceed to Section A.
 No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

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

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
 Disease/condition does not exist in children
 Too few children with disease to study
 There are safety concerns
 Other: _____

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

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

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

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

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

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

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

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

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

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

NDA 21-150/S-007

Page 3

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

**FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH
STAFF at 301-796-0700**

(Revised: 10/10/2006)

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Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: _____

Is this an orphan indication?

- Yes. PREA does not apply. Skip to signature block.
- No. Please proceed to the next question.

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

- Yes: Please proceed to Section A.
- No: Please check all that apply: ___Partial Waiver ___Deferred ___Completed
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: _____

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

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below)::

Min _____	kg _____	mo. _____	yr. _____	Tanner Stage _____
Max _____	kg _____	mo. _____	yr. _____	Tanner Stage _____

Reason(s) for partial waiver:

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

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is

complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below)::

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

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

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

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

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 10/10/2006)

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

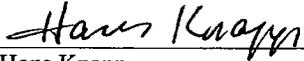
/s/

Elaine Abraham
11/8/2007 01:59:35 PM

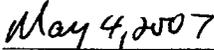
Supplemental NDA 21-150/S-007: Zyrtec-D 12 Hour (Cetirizine HCl 5 /Pseudoephedrine HCl 120 mg)
Over-the-Counter (OTC) Use
Item 9 Safety Update

16. DEBARMENT CERTIFICATION [FD&C Act 306(K)(1)]

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



Hans Knapp
Director, Global Regulatory Affairs
McNeil Consumer Healthcare



May 4, 2007

4 Page(s) Withheld

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 Draft Labeling

 Deliberative Process

Withheld Track Number: Administrative

DEPARTMENT OF HEALTH AND HUMAN SERVICES Food and Drug Administration	Form Approved: OMB No. 0910-0396 Expiration Date: April 30, 2009 NDA Number : 21-150
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 check box.

- (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 (See attached.)

- (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.

Clinical investigators (See attached.)

NAME	JOHN J. REGAN	TITLE	SR. DIRECTOR - MEDICAL FIN
FIRM/ORGANIZATION	Pfizer Inc		
SIGNATURE	<i>John J. Regan</i>	DATE	November 9, 2006

<p>Paperwork Reduction Act Statement</p> <p>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. 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:</p>	Department of Health and Human Services Food and Drug Administration 5600 Fishers Lane, Room 14C-03 Rockville, MD 20857
---	--

FORM FDA 3454 (4/06)

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 Deliberative Process

Withheld Track Number: Administrative-_____

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: April 30, 2009
NDA Number : 21-150

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

TO BE COMPLETED BY APPLICANT

The following information concerning who participated as a clinical investigator in the submitted study

is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

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

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

NAME	<i>JOHN J. REGAN</i>	TITLE	<i>SR. DIRECTOR - MEDICAL FINANCE</i>
FIRM/ORGANIZATION	<i>PFIZER INC</i>		
SIGNATURE	<i>John J. Regan</i>	DATE	<i>November 9, 2006</i>

Paperwork Reduction Act Statement

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

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

FORM FDA 3455 (4/06)

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Withheld Track Number: Administrative-

DEPARTMENT OF HEALTH AND HUMAN SERVICES Food and Drug Administration DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS.	Form Approved: OMB No. 0910-0396 Expiration Date: April 30, 2009 NDA Number : 21-150
TO BE COMPLETED BY APPLICANT	

The following information concerning Name of clinical investigator
 who participated as a clinical investigator in the submitted study

Name of clinical study

is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable check boxes.

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

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

NAME <i>John J. Regan</i>	TITLE <i>SR. DIRECTOR - MEDICAL FINANC</i>
FIRM/ORGANIZATION <i>Pfizer Inc</i>	
SIGNATURE <i>John J. Regan</i>	DATE <i>November 9, 2006</i>

Paperwork Reduction Act Statement
 An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 4 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to:
 Department of Health and Human Services
 Food and Drug Administration
 5600 Fishers Lane, Room 14-72
 Rockville, MD 20857

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 Draft Labeling

 Deliberative Process

Withheld Track Number: Administrative

OTC Drug Labeling Review

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

Center for Drug Evaluation and Research • Food and Drug Administration

NDA 2nd Addendum Labeling Review

NDA # 21-150; SE6 (007)

Submission Date : 10/30/07 and 11/06/07

Review Date : 11/08/07

Applicant: McNeil Consumer Healthcare Inc.
201 Tabor Road
Morris Plains, New Jersey 07950

Applicant's Representative: Hans Knapp
Director, Global Regulatory Affairs
215-273-7000; 973-385-7250

Drug: Zyrtec-D
(Cetirizine HCl 5 mg / Pseudoephedrine HCl 120 mg)
Extended Release Tablets

Pharmacological Category: Antihistamine/Nasal decongestant

Submitted:

- A. 10/30/07 Submission: Draft labeling for the following:
1. 1-count individual blister
 2. 50-count sample packet dispenser
 3. 1-count blister packet (sample)
 4. 12-count carton
 5. 24-count carton FDM and CLUB (different NDC numbers only)
 6. Drug Facts annotated specifications
- B. 11/06/07 Submission: Representative draft labeling for the following:
1. 1-count blister packet
 2. 12-count carton

Background:

On October 30, 2007, the sponsor submitted revised draft labeling for Zyrtec-D Extended Release Tablets (cetirizine 5 mg / pseudoephedrine 120 mg) in response to the Agency's Information Request Letter dated October 25, 2007. In the letter, the Agency requested that the statement "Indoor & Outdoor" be revised _____ and be relocated to appear either above the product name or under the "statement of identity". The Agency also requested that the statement be moved away from the promotional phrase "*12 hour Relief of • Sneezing • Runny Nose • Itchy, Watery Eyes • Itchy Throat or Nose • Sinus Pressure • Nasal Congestion*".

During a subsequent telephone call to the sponsor on November 5, 2007, the Agency indicated that the sponsor needs to revise the Drug Facts and non-Drug Facts "Uses" sections of all Zyrtec-D SKUs

The Agency agreed that the sponsor could submit representative labeling that included the revised Drug Facts and non-Drug Facts "Uses" section for its review and comment. However, the sponsor needed to certify that the Drug Facts and non-Drug Facts "Uses" section for all other Zyrtec-D SKUs will be revised as requested by the Agency.

On November 6, 2007, the sponsor submitted representative draft labeling for the 1-count sample blister packet and the 12-count carton that included the revised Drug Facts and non-Drug Facts "Uses" section as requested by the Agency. The sponsor also certified that the "Uses" sections, as proposed in the labeling of the sponsor's October 30, 2007 Amendment to NDA 21-150/S-007 (Zyrtec-D), will be revised to reflect the Agency's requested labeling changes.

Reviewer Comments:

1. The sponsor has revised the labeling of all Zyrtec-D SKUs as requested in the Agency's October 25, 2007 Information Request Letter. These labeling changes are acceptable.
2. The sponsor has certified that there have been no changes to the Drug Facts annotated specifications since that submitted in its October 12, 2007 submission. This is acceptable.
3. The revised Drug Facts and non-Drug Facts "Uses" sections in the representative labeling submitted in the sponsor's November 6, 2007 submission (i.e., 1-count blister packet and the 12-count carton) are acceptable.
4. The sponsor certifies that the "Uses" sections, as proposed in the labeling submitted by the sponsor on October 30, 2007, is being revised for all Zyrtec-D labeling to reflect the Agency's labeling changes requested during the telephone conversation on November 5, 2007. The sponsor further indicates that this change will be made prior to the initial introduction of the product into the marketplace. This is acceptable.

Recommendations:

1. An approval letter can be issued to the sponsor requesting final printed labeling for the following SKUs:
 - *1-count sample blister packet and 12-count carton:* Final printed labeling must be identical to labeling submitted on November 6, 2007
 - *1-count individual blister, 24-count FDM and Club cartons, and 50-count packet dispenser:* Final printed labeling identical to the labeling submitted on October 30, 2007, except that the labeling for these SKUs must include the revised Drug Facts and non-Drug Facts "Uses" sections as submitted in the representative labeling on November 6, 2007.
2. Inform the sponsor that the flag "NEW!", wherever it appears in the labeling of all acceptable SKUs, needs to be deleted 6 months after introduction into the OTC market.

Cazemiro R. Martin
Reg. Review Chemist

Concur: Matthew Homan, Ph.D.
Team Leader

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/s/

Cazemiro Martin
11/8/2007 10:46:07 AM
INTERDISCIPLINARY

Matthew Holman
11/8/2007 10:58:16 AM
INTERDISCIPLINARY



November 6, 2007

Leah Christl, Ph.D.
Supervisory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Road
Room 5480
Beltsville, MD 20705-1266

**Re: Supplemental NDA 21-150/S-007: Zyrtec-D
(Cetirizine HCl 5 mg/Pseudoephedrine HCl 120 mg)
Over-the-Counter (OTC) Use**

Subject: Amendment to a Pending Application

Dear Dr. Christl:

McNeil Consumer Healthcare, Division of McNeil-PPC, Inc. is submitting the final draft labeling for NDA 21-150/S-007 in response to the Agency's labeling changes requested via conference call on November 5, 2007.

Per the Agency's request, McNeil certifies that the "Uses", as proposed in the labeling in our October 30, 2007 Amendment to a Pending Application for NDA 21-150/S-007 (Zyrtec-D), is being revised to reflect the Agency's changes. The revised "Uses" will read as follows:

Uses

- temporarily relieves these symptoms due to hay fever or other upper respiratory allergies:
 - runny nose
 - sneezing
 - itchy, watery eyes
 - itching of the nose or throat
 - nasal congestion
- reduces swelling of nasal passages
- temporarily relieves sinus congestion and pressure
- temporarily restores freer breathing through the nose

39 Page(s) Withheld

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4 Draft Labeling

 Deliberative Process



DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Office of New Drugs - Immediate Office
Pediatric and Maternal Health Staff
Silver Spring, MD 20993
Telephone 301-796-2200
FAX 301-796-9744

M E M O R A N D U M

DATE: October 5, 2007

FROM: Felicia Collins, MD, MPH, Medical Officer
Pediatric and Maternal Health Staff, Office of New Drugs

THROUGH: Lisa Mathis, MD, OND Associate Director
Pediatric and Maternal Health Staff, Office of New Drugs

TO: Andrea Leonard-Segal, MD, Director
Division of Nonprescription Clinical Evaluation,
Office of Nonprescription Products (ONP)

RE: PREA Requirements for Rx-to-OTC Switch

Drug: Zyrtec-D[®]
(cetirizine HCL 5 mg/pseudoephedrine HCL 120 mg)

Dosage Form: Extended release tablet

Administration Route: Oral

Sponsor: McNeil

Indication: (current Rx) Relief of nasal and non-nasal symptoms
associated with seasonal or perennial allergic rhinitis in adults
and children 12 years of age and older

Application: NDA 21-150, SE6-007

Division's Consult Comments

ONP requests Pediatric and Maternal Health Staff (PMHS) review and comment as to whether a [partial] pediatric waiver should be granted for the proposed Zyrtec-D[®] Rx-to-OTC switch [for children under 12 years old]. Cetirizine is a second generation antihistamine and is a NDA prescription product. Pseudoephedrine is a decongestant which is available OTC. The amount of pseudoephedrine in the combination product exceeds the amount allowed by the OTC monograph for children under 12 years old.

On September 18, 2007, the Division Medical Team Leader (Daiva Shetty) clarified that her questions are whether the Division needs to ask for a Zyrtec-D[®] pediatric formulation and what kinds of studies would the Division ask the Sponsor to conduct.

Materials Reviewed

- Zyrtec-D[®] Rx drug labeling, March 17, 2004
- FDA approval letter for Rx Zyrtec-D[®], August 10, 2001
- OTC Monograph for Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use, 21 CFR 340
- Division of Nonprescription Clinical Evaluation (Division) consult information, June 1, 2007
- E-mails from the Division Project Manager, Medical Officer, Medical Team Leader, and Interdisciplinary Scientist and the Division of Allergy and Pulmonary Products (DPAP) Medical Officer, September 2007

Background

Product Description

Zyrtec-D[®] is a combination product composed of cetirizine and pseudoephedrine. Cetirizine, a metabolite of hydroxyzine, is an antihistamine having principal effects mediated via selective inhibition of H₁ receptors. Pseudoephedrine hydrochloride is an orally active sympathomimetic amine that exerts a decongestant action on the nasal mucosa and a recognized effective agent for the relief of nasal congestion due to allergic rhinitis.

Regulatory History

Zyrtec-D[®] (cetirizine 5 mg/pseudoephedrine 120 mg dosed BID) was first approved in August 10, 2001 for adults and children 12 years of age and older *for the relief of nasal and non-nasal symptoms associated with seasonal or perennial allergic rhinitis*. The FDA approval letter noted that the Sponsor had fulfilled the pediatric study requirement for patients 12 years of age and older at that time and that a waiver for studies in patients below 12 years of age had been granted. According to the DPAP Medical Officer (Susan Limb), at the time of the original approval, DPAP granted a partial waiver of pediatric studies required under the Pediatric Research Equity Act (PREA) because: (1) the dose of pseudoephedrine in Zyrtec-D[®] exceeded the recommended dosing for children under the age of 12; and (2) there were other existing treatments for both cetirizine and pseudoephedrine available down to the age of 2 years. The Pediatric Use Section of the drug labeling states that “the dose of pseudoephedrine exceeds the recommended dose for pediatric patients under 12 years of age. Therefore, clinical trials of Zyrtec-D[®] have not been conducted in patients under 12 years of age.”

On January 10, 2007, the Sponsor submitted a supplemental NDA requesting an Rx-to-OTC switch for Zyrtec-D[®]. According to a September 17, 2007 e-mail from the Division Project Manager (Elaine Abraham), the proposed Uses Section of Drug Facts would state that the product:

- *Temporarily relieves [the following] symptoms due to hay fever or other upper respiratory allergies: runny nose, sneezing, itchy or watery eyes, itching of the nose or throat;*
- *Provides relief of the above symptoms due to _____ upper respiratory allergies (such as dust mites, animal dander, and molds) and _____ upper respiratory allergies (such as ragweed, grass, and tree pollens);*
- *Temporarily relieves nasal congestion due to _____ hay fever or other upper respiratory allergies;*
- *Reduces swelling of nasal passages;*
- *Temporarily relieves sinus congestion and pressure; and*
- *Temporarily restores freer breathing through the nose.*

_____ According to the Division's interdisciplinary scientist working on this product (Cazemiro Martin), because there is no healthcare professional generally available in the OTC setting to instruct consumers on how to take their OTC drug product, for OTC NDA drug products, the Division always includes all the indications as stated in the applicable OTC drug monograph to prevent medication errors due to multiple product use with the same active ingredient.

Since the amount of pseudoephedrine in the combination exceeds the amount allowed by the OTC monograph for children < 12 years old (see Discussion section below), the Sponsor is asking for a partial waiver of pediatric studies required under PREA for children < 12 years old.

The Division's deadline for completing the review of the supplemental NDA is November 11, 2007.

Discussion

Criteria for a Partial Waiver of Pediatric Studies Required Under PREA

PREA (21 USC 355c) requires sponsors to submit pediatric assessments when they submit an application or supplemental application for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration. Per 21 USC 355c(a)(4), the assessment requirements may be waived "with respect to a specific pediatric population if the applicant certifies and the Secretary finds that--

- (i) Necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed);
- (ii) There is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in that age group;
- (iii) The drug or biological product --
 - (I) Does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in that age group; and
 - (II) Is not likely to be used by a substantial number of pediatric patients in that age group; or
- (iv) The applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed.

... If a waiver is granted because there is evidence that the drug or biological product would be ineffective or unsafe in pediatric populations, the information shall be included in the labeling for the product." These provisions were maintained by the recent passage of PREA of 2007.

It appears that the Sponsor's partial waiver request relates to the waiver criteria that the drug in its current formulation would be unsafe in children < 12 years old. It is unclear to this reviewer if the Sponsor has considered developing a formulation appropriate for pediatric patients < 12 years old.

Pediatric Labeling for Cetirizine and Pseudoephedrine As Single Agents

Cetirizine's safety has been demonstrated in pediatric patients 6 months to 11 years old according to the drug labeling. Cetirizine's effectiveness claim for the treatment of allergic rhinitis in pediatric patients 6 months to 11 years old is based on an extrapolation of the demonstrated efficacy of cetirizine in adults with this condition and the likelihood that the disease course, pathophysiology, and the drug's effect are substantially similar between adults and children. Efficacy was extrapolated down to 6 months of age for perennial allergic rhinitis and down to 2 years of age for seasonal allergic rhinitis, because these diseases are thought to occur down to these ages in children. The cetirizine dosing regimen is:

- ≥ 12 years old: 5 – 10 mg/day;
- 6 to < 12 years old: 5 – 10 mg;
- 2 to < 6 years old: 2.5 - 5 mg/day; and
- 6 months to < 2 years old: 2.5 mg/day (can be increased to 5 mg/day in children 12 to 23 months old).

For pseudoephedrine, the drug labeling is based on the OTC monograph for nasal decongestant drugs (21 CFR 341.80). Per 21 CFR 341.80(b), nasal decongestant uses may include:

- Temporarily relieves nasal congestion (due to the common cold, hay fever, or other upper respiratory allergies (allergic rhinitis) or associated with sinusitis);
- Temporarily relieves nasal stuffiness;
- Reduces swelling of nasal passages, shrinks swollen membranes;
- Temporarily restores freer breathing through the nose;
- Helps decongest sinus openings and passages, temporarily relieves sinus congestion and pressure; and
- Promotes nasal and/or sinus drainage, temporarily relieves sinus congestion and pressure.

Per the OTC monograph (21 CFR 341.80(d)(1)(ii)), the pseudoephedrine dosing regimen is:

- ≥ 12 years old: 60 mg every 4 – 6 hours not to exceed 240 mg/day;
- 6 to < 12 years old: 30 mg every 4 – 6 hours not to exceed 120 mg/day;
- 2 to < 6 years old: 15 mg every 4 – 6 hours not to exceed 60 mg/day; and
- < 2 years old: consult a doctor.

According to the approved dosing for cetirizine and pseudoephedrine as single agents, the existing Zyrtec-D® formulation (cetirizine 5 mg/pseudoephedrine 120 mg dosed BID for a total dose of cetirizine 10 mg/day and pseudoephedrine 240 mg/day):

- 1) exceeds the approved cetirizine dosing for children < 6 years old (i.e., 2.5 – 5 mg/day); and
- 2) exceeds the approved pseudoephedrine dosing for children < 12 years old (i.e., not to exceed 120 mg/day).

FDA Advisory Committee Meeting on Cold and Cough Product Use in Children

A joint meeting of the FDA Nonprescription Drugs Advisory Committee and the Pediatric Advisory Committee is scheduled for October 18 and 19, 2007 to discuss the safety and efficacy of OTC cough and cold products marketed for pediatric use. A citizen petition was submitted to the FDA on March 1, 2007 that raised concerns about the safety and efficacy of cough and cold products in children under 6 years of age. The petition requested that the FDA amend the OTC Drug Monograph for Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products (i.e., 21 CFR 341) to require that labeling for OTC antitussive, expectorant, nasal decongestant, antihistamine, and combination cough and cold products states that these products: (1) have not been found to be safe or effective in children under 6 years of age for the treatment of cough and cold; and (2) should not be used for the treatment of cough and cold in children under 6 years of age.

Conclusions and Recommendations

The Sponsor's other proposed OTC uses can be linked to the Rx indications of seasonal or perennial allergic rhinitis.

PMHS anticipates that the discussion from the October 2007 FDA Advisory Committee Meeting on OTC cold and cough products for pediatric use will be germane to the question as to whether pediatric studies should be required for Zyrtec-D®, the type(s) of pediatric studies that should be required, and in which pediatric population(s) should these studies be conducted. However, PMHS also acknowledges the Division's November 11, 2007 date for completing the review of this supplemental NDA.

Therefore, PMHS recommends that the Division:

- 1) Grant a partial waiver of PREA studies in children < 2 years old (In DPAP's review of cetirizine, it concluded that seasonal and perennial allergic rhinitis occur in pediatric patients ≥ 2 years old and ≥ 6 months old, respectively. Thus, in the OTC setting where there may not be a healthcare professional involved in patient diagnosis, it appears appropriate to limit cetirizine use to pediatric populations patients ≥ 2 years old); and
- 2) Defer pediatric studies for children 2 to < 12 years old, to include the development of an age appropriate formulation, studies and/or data to support pediatric dosing, and studies to support safety and efficacy.

If the Advisory Committee recommends that cold and cough products should not be used in a specific pediatric population due to safety concerns, the Division later can waive PREA studies in that pediatric population to be consistent with the Advisory Committee's recommendations. Please note that if the Division ultimately determines that PREA studies should be partially waived for a particular pediatric population due to safety concerns, the relevant safety information must be included in the OTC drug labeling.

In addition, if it has not done so already, the Sponsor should formally request a partial waiver of pediatric studies required under PREA and include a justification(s) consistent with the criteria listed in PREA of 2007.

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/s/

Felicia Collins
10/9/2007 08:43:36 AM
MEDICAL OFFICER

Lisa Mathis
10/22/2007 04:58:48 PM
MEDICAL OFFICER



DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Office of New Drugs - Immediate Office
Pediatric and Maternal Health Staff
Silver Spring, MD 20993
Telephone 301-796-2200
FAX 301-796-9744

ADDENDUM TO MEMORANDUM

DATE: November 6, 2007
Original memo dated September 2007

FROM: Lisa Mathis, MD, OND Associate Director
Pediatric and Maternal Health Staff, Office of New Drugs

TO: Andrea Leonard-Segal, MD, Director
Division of Nonprescription Clinical Evaluation,
Office of Nonprescription Products (ONP)

RE: PREA Requirements for Rx-to-OTC Switch

Drug: Zyrtec-D[®]
(cetirizine HCL 5 mg/pseudoephedrine HCL 120 mg)

Dosage Form: Extended release tablet

Administration Route: Oral

Sponsor: McNeil

Indication: (current Rx) Relief of nasal and non-nasal symptoms
associated with seasonal or perennial allergic rhinitis in adults
and children 12 years of age and older

Application: NDA 21-150, SE6-007

Please see original memo from Felicia Collins, MD, MPH, Medical Officer, Pediatric and Maternal Health Staff, Office of New Drugs from September 2007 for additional information.

Division's Original Consult Question:

ONP requested Pediatric and Maternal Health Staff (PMHS) review and comment as to whether a [partial] pediatric waiver should be granted for the proposed Zyrtec-D[®] Rx-to-OTC switch [for children under 12 years old]. Cetirizine is a second generation antihistamine and is a NDA prescription product. Pseudoephedrine is a decongestant which is available OTC. The amount of pseudoephedrine in the combination product exceeds the amount allowed by the OTC monograph for children under 12 years old.

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/s/

Lisa Mathis
11/6/2007 07:56:44 PM
MEDICAL OFFICER



NDA 21-150/S-007

INFORMATION REQUEST LETTER

McNeil Consumer Healthcare
Attention: Robert Kohler
Senior Director, Global Regulatory Affairs
U.S. Agent for Pfizer, Inc.
201 Tabor Road
Morris Plains, NJ 07950

Dear Mr. Kohler:

Please refer to your January 10, 2007 supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zyrtec-D 12 Hour (cetirizine HCl 5 mg/pseudoephedrine HCl 120 mg) tablets.

We also refer to your submission dated October 12, 2007.

We are reviewing the labeling section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. Revise and resubmit draft labeling for the following SKUs for our review:
 - 50-count sample packet dispenser
 - 1-count blister packet
 - 12-count carton
 - 24-count carton FDM and CLUB (different NDC numbers only)
2. Revise the labeling for the above SKUs for accuracy and clarity as follows:
 - a. Revise the phrase "Indoor & Outdoor" to read _____ wherever it appears in the labeling (*italic is added for emphasis only*).
 - b. Relocate the revised phrase _____ on the PDP and side panels, wherever it appears in the labeling, to appear either above the product's proprietary name, or beneath the "statement of identity" section. This revised phrase must be distant from the promotional phrase "*12 hour Relief of • Sneezing • Runny Nose • Itchy, Watery Eyes • Itchy Throat or Nose • Sinus Pressure • Nasal Congestion*".
3. You do not need to resubmit "Drug Facts" annotated specifications if you certify that there are no changes to these specifications.

4. Your revised labeling should include only the changes described above and no additional changes.

In addition to sending the revised labeling of these SKUs to your NDA, you should email or fax a copy to Elaine Abraham. These should be received by us at least one week prior to the action due date, that is by November 2, 2007, in order to allow time for our review.

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

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Leah Christl

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OTC Drug Labeling Review

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

Center for Drug Evaluation and Research • Food and Drug Administration

NDA Addendum Labeling Review

NDA # 21-150; SE6 (007)

Submission Date : 10/12/07

Review Date : 10/24/07

Applicant: McNeil Consumer Healthcare Inc.
201 Tabor Road
Morris Plains, New Jersey 07950

Applicant's Representative: Hans Knapp
Director, Global Regulatory Affairs
215-273-7000; 973-385-7250

Drug: Zyrtec-D
(Cetirizine HCl 5 mg / Pseudoephedrine HCl 120 mg)
Extended Release Tablets

Pharmacological Category: Antihistamine/Nasal decongestant

Submitted: Draft labeling for the following:

1. 1-count individual blister
2. 50-count sample packet dispenser
3. 1-count blister packet (sample)
4. 12-count carton
5. 24-count carton FDM and CLUB (different NDC numbers only)
6. Drug Facts annotated specifications

Background:

In this submission, the sponsor has submitted revised draft labeling for Zyrtec-D Extended Release Tablets (cetirizine 5 mg / pseudoephedrine 120 mg). The revised labeling is based on the Agency's Information Request Letter dated August 29, 2007, which requested changes to the sponsor's proposed labeling. The sponsor has also included draft labeling for a 24-count carton designated "FDM" and another 24-count carton designated "CLUB".

At the request of the sponsor, a telephone conference call on September 12, 2007 was held during which the Agency discussed the proposed labeling changes included in its Information Request Letter. During the discussion, the Agency mentioned that it would provide further comment at a later date regarding the statement in the Drug Facts "Uses" section _____

_____ The sponsor retained the reference to "Indoor and Outdoor" on the PDP and other side panels. The sponsor also explained that the only difference between the 24-count "FDM" and the 24-count "CLUB" is the assigned NDC number.

Reviewer Comments:

1. The sponsor indicated that the proprietary name for this product is "Zyrtec-D". There are no other name extensions (e.g., "Allergy & Congestion" or "12-Hour") as part of the proprietary name.
2. The sponsor has revised the labeling of this product based on the labeling revisions included in the Agency's Information Request Letter (dated August 29, 2007) and has deleted reference to _____ allergies in the Drug Facts "Uses" section as previously agreed upon.

3. Draft labeling for the 1-count individual blister is acceptable.

4. The draft labeling for the following is not acceptable:

- 50-count sample packet dispenser
- 1-count blister packet
- 12-count carton
- 24-count carton FDM and CLUB (different NDC numbers only)

The sponsor needs to further revise the labeling for accuracy and clarity as follows:

- a. Revise the phrase "Indoor & Outdoor" to read _____ wherever it appears in the labeling.
- b. Relocate the revised phrase _____ on the PDP and side panels, wherever it appears in the labeling, to appear either above the product's proprietary name, or beneath the "statement of identity" section. This revised phrase must be distant from the promotional phrase "*12 hour Relief of Sneezing • Runny Nose • Itchy, Watery Eyes • Itchy Throat or Nose • Sinus Pressure • Nasal Congestion*".

5. Drug Facts annotated specifications are acceptable.

6. The sponsor indicated in this submission that it has removed the package insert originally proposed on January 10, 2007 for use with this product. This is acceptable.

Recommendations:

1. An approval letter can be issued to the sponsor requesting final printed labeling for the 1-count individual blister. This final printed labeling must be identical to the labeling submitted in this submission.

2. The labeling of the following is not acceptable.

- 50-count sample packet dispenser
- 1-count blister packet
- 12-count carton
- 24-count carton FDM and CLUB (different NDC numbers only)

The sponsor needs to further revise the labeling for accuracy and clarity as follows:

- a. Revise the phrase "Indoor & Outdoor" to read _____ wherever it appears in the labeling.
- b. Relocate the revised phrase " _____ on the PDP and side panels, wherever it appears in the labeling, to appear either above the product's proprietary name, or beneath the "statement of identity" section. This revised phrase must be distant from the promotional phrase "*12 hour Relief of Sneezing • Runny Nose • Itchy, Watery Eyes • Itchy Throat or Nose • Sinus Pressure • Nasal Congestion*".

Inform the sponsor to further revise the labeling of these SKUs as stated above and resubmit revised draft labeling for our review and comment, prior to the Action Due date. The sponsor does not need to resubmit "Drug Facts" annotated specifications if it certifies that there are no changes to these specifications.

3. Inform the sponsor that the flag "NEW!", wherever it appears in the labeling of all acceptable SKUs, needs to be deleted 6 months after introduction into the OTC market.

Cazemiro R. Martin
Reg. Review Chemist

Concur: Marina Chang, R.Ph.
Team Leader

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/s/

Cazemiro Martin
10/24/2007 12:57:24 PM
INTERDISCIPLINARY

Marina Chang
10/24/2007 02:18:00 PM
INTERDISCIPLINARY



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-150/S-007

INFORMATION REQUEST LETTER

McNeil Consumer Healthcare
Attention: Robert Kohler
Senior Director, Global Regulatory Affairs
U.S. Agent for Pfizer, Inc.
201 Tabor Road
Morris Plains, NJ 07950

Dear Mr. Kohler:

Please refer to your January 10, 2007 supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zyrtec-D 12 Hour (cetirizine HCl 5 mg/pseudoephedrine HCl 120 mg) Tablets.

We also refer to your submission dated July 11, 2007.

We are reviewing the labeling section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. Revise and resubmit revised labels with annotated Drug Facts specifications for our review as follows:

a. 1-count blister pouch (sample), 50-count sample packet dispenser, 1-count blister package, and 12-count carton:

- i. Identify the proprietary name for this product. We are not sure if the proprietary name is:
 - Zyrtec-D (appears on the proposed PDP)
 - Zyrtec-D 12 Hours (as stated on the title of the cover letter and FDA Form 356(h))
 - Zyrtec-D Allergy & Congestion (as stated in the cover letter and throughout the submission)

If the phrase "Allergy & Congestion" or "12 Hour" is part of the proprietary name, the phrase must be relocated to appear in close proximity to and in the same color as the brand name "Zyrtec-D", followed by the active ingredient, potency, and pharmacological category. The same proprietary name will need to appear on all SKUs wherever the brand name "Zyrtec-D" appears in the labeling.

- ii. Relocate the phrase "Extended Release Tablets" to appear as part of the statement of identity. For example:
Zyrtec-D
(Cetirizine HCl 5 mg /antihistamine; Pseudoephedrine HCl 120 mg/ nasal decongestant)
Extended Release Tablets
 - iii. Add the phrase ' _____' wherever the word "Tablet" appears in the labeling.
- b. Provide for lot number and expiration date for the 50-count and 12-count.
 - c. **1-count blister pouch:** The "Drug Facts" information is not in compliance with 21 CFR 201.66 (i.e., format requirements). The presentation of this information is acceptable if you remove the heading "Drug Facts". Use of the "Drug Facts" title to introduce this information requires full compliance with labeling content and format requirements as set forth in 21 CFR 201.66.
 - d. **Drug Facts:** For all SKUs, revise per attached prototype "Drug Facts" labeling.
2. The flags "*Full Prescription Strength*" and "*Full Prescription Strength...Now OTC!*" are not acceptable. These flags must be deleted or revised _____ wherever they appear in the labeling of Zyrtec-D.
 3. To make the established names of the active ingredients, dosage forms, and pharmacological categories information for all SKUs more prominent, we recommend the following:
 - a. increase the type size and the color contrast lettering of the active ingredients, dosage forms, and pharmacological categories to make more readable.
 - b. use a more distinguishable graphic feature (e.g., print or color feature) to highlight the dosage strengths (i.e., "5 mg / 120 mg") of the two active ingredients wherever stated in the labeling.
 4. We remind you to submit the draft 24-count carton label for our review as you stated in your August 9, 2007 email.

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

Enclosure: - Prototype "Drug Facts" labeling

1 Page(s) Withheld

 Trade Secret / Confidential

 8 Draft Labeling

 Deliberative Process

Withheld Track Number: Administrative

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/s/

Leah Christl
8/29/2007 08:50:10 AM

OTC Drug Labeling Review

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

Center for Drug Evaluation and Research • Food and Drug Administration

NDA Supplement Labeling Review

NDA # 21-150; SE6 (007)

Submission Date : 1/10/07 and 7/11/07

Review Date : 8/27/07

Applicant: McNeil Consumer Healthcare Inc.
201 Tabor Road
Morris Plains, New Jersey 07950

Applicant's Representative: Robert Kohler
Senior Director, Global Regulatory Affairs
215-273-7000; 973-385-7250

Drug: Zyrtec-D
(Cetirizine HCl 5 mg / Pseudoephedrine HCl 120 mg)
Extended Release Tablets

Pharmacological Category: Antihistamine/Nasal decongestant

Submitted: Draft labeling for the following:

1. 1-count blister pouch (sample)
2. 50-count sample packet dispenser
3. 1-count blister packet
4. 12- and 24-count carton
5. Drug Facts annotated specifications

Background:

This product was approved on August 10, 2001 for prescription marketing for the relief of nasal and non-nasal symptoms associated with seasonal or perennial allergic rhinitis in adults and children 12 years of age and older.

On January 10, 2007, the sponsor submitting an Rx-to-OTC switch efficacy supplement. The proposed OTC Zyrtec-D product will be mainly indicated for temporary relief of symptoms of hay fever and other upper respiratory allergies and for relief of nasal congestion due to _____ hay fever, or other upper respiratory allergies. The initial submission included draft labeling for the 1-count blister pouch (sample), 60-count sample packet dispenser, 1-count blister packet, 12-count carton (individual blisters), and a patient package insert.

On July 11, 2007, the sponsor resubmitted revised draft labeling for proposed OTC Zyrtec-D and pointed out that no changes were made to the Drug Facts labeling as proposed in the January 10, 2007 submission. However, the sponsor indicated the following:

1. package insert is removed
2. addition of a 24-count carton SKU. Note: The sponsor did not include the 24-count carton draft labeling in this submission as was stated in its summary section.
3. 50-count sample packet dispenser replaces the originally proposed 60-count dispenser .

Reviewer Comments:

1. **PDP** -All SKUs: [1-count blister pouch (sample), 50-count sample packet dispenser, and 12-count carton]

(a) The proprietary name for this product is not clear. The sponsor needs to inform the agency of the intended proprietary name. The proprietary names stated in this submission include:

- Zyrtec-D : appears on the proposed PDP
- Zyrtec-D 12 Hours: stated on the title of the cover letter and FDA Form 356(h)
- Zyrtec-D Allergy & Congestion: stated in the cover letter and throughout the submission

If the phrase "Allergy & Congestion" or "12 hour" is part of the proprietary name, the phrase must be relocated to appear in close proximity to and in the same color as the brand name "Zyrtec-D", followed by the active ingredient, potency, and pharmacological category. The same proprietary name will need to appear on all SKUs wherever the brand name "Zyrtec-D" appears in the labeling.

(b) The established names of the active ingredients, dosage forms, and pharmacological categories need to appear more prominently. It is recommended that the sponsor:

- i. increase the color contrast lettering of this information and increase the font size to make the established names and pharmacological categories more readable.
- ii. use a more prominent graphic feature (e.g., print or color feature) to highlight the dosage strengths (i.e., "5 mg / 120 mg") of the two active ingredients stated in this section.

(c) The sponsor needs to:

- i. relocate the phrase "Extended Release Tablets" to appear as part of the statement of identity of this product. For example:

Zyrtec-D
(Cetirizine HCl 5 mg/antihistamine; Pseudoephedrine HCl 120 mg/ nasal decongestant)
Extended Release Tablets

- ii. add the phrase _____ wherever the word "Tablet" appears in the labeling of this product.

2. **Other Panel**: 50-count sample packet dispenser and 12-count carton: Provisions for lot number and expiration date are needed.

3. **Drug Facts Information**: [All SKUs]

(a) After the heading "*Active ingredients (in each tablet)*", the sponsor needs to revise the parenthetical expression _____ for accuracy and labeling consistency.

(b) **Uses**: The second bulleted statement under this heading should be revised to read as follows:

(c) **Under the subheading "Ask a doctor before use if you have"**

- i. add the bulleted statement _____. Pseudoephedrine is contraindicated in patients with narrow-angle glaucoma.
- ii. immediately after the bulleted statement "liver or kidney disease", the following statement needs to appear: _____ This statement appears in the labeling of this class of OTC drug products.

(d)

(e) **"If pregnant or breast-feeding"** warning: Revise this warning as follows: _____

This revision reflects the Rx

labeling that recommends nursing mothers not to use this product.

- (f) **Under the heading “Directions”**, the sponsor needs to add as the first bulleted statement the following text: “_____ This information, which appears in the Rx labeling, advises consumers how to properly take this extended release tablet.
- (g) For the **1-count blister pouch**:
- See comments 2(a) through (e) above.
 - The “Drug Facts” information is not in compliance with 21 CFR 201.66 (i.e., format requirements). The presentation of this information is acceptable if the sponsor removes the heading “Drug Facts”. Use of the “Drug Facts” title to introduce this information requires full compliance with labeling content and format requirements as set forth in 21 CFR 201.66.
4. **Flags**:
- The flag “New”, wherever it appears in the labeling, must be deleted 6 months after introduction into the OTC market.
 - The flags “*Full Prescription Strength*” and “*Full Prescription Strength...Now OTC!*” are not acceptable. These flags must be deleted or revised _____, wherever they appear in the labeling of Zyrtec-D.
5. **1-count blister package**:
- See comment 1(a) above.
 - The sponsor needs to add the dosage form “Extended Release Tablets” as part of the statement of identity.
 - It is recommended that the sponsor make more prominent the dosage strengths (i.e., “5 mg / 120 mg”) of the two active ingredients.
6. **Drug Facts annotated specifications**: Acceptable.

Recommendations:

- This application is not approvable. Inform the sponsor to revise and resubmit revised labels with annotated Drug Facts specifications for our review and comment prior to the Action Due date as follows:

A. 1-count blister pouch (sample), 50-count sample packet dispenser, 1-count blister package, and 12-count carton:

- Identify the proprietary name for this product. We are not sure if the proprietary name is:
 - Zyrtec-D (appears on the proposed PDP)
 - Zyrtec-D 12 Hours (as stated on the title of the cover letter and FDA Form 356(h))
 - Zyrtec-D Allergy & Congestion (as stated in the cover letter and throughout the submission)

If the phrase “Allergy & Congestion” or “12 Hour” is part of the proprietary name, the phrase must be relocated to appear in close proximity to and in the same color as the brand name “Zyrtec-D”, followed by the active ingredient, potency, and pharmacological category. The same proprietary name will need to appear on all SKUs wherever the brand name “Zyrtec-D” appears in the labeling.

- Relocate the phrase “Extended Release Tablets” to appear as part of the statement of identity. For example:

Zyrtec-D
(Cetirizine HCL 5 mg /antihistamine; Pseudoephedrine HCL 120 mg/ nasal decongestant)
Extended Release Tablets

- Add the phrase _____ wherever the word “Tablet” appears in the labeling
- B.** Provisions for lot number and expiration date for the 50-count and 12-count are needed.

- C. **1-count blister pouch:** The “Drug Facts” information is not in compliance with 21 CFR 201.66 (i.e., format requirements). The presentation of this information is acceptable if the sponsor removes the heading “Drug Facts”. Use of the “Drug Facts” title to introduce this information requires full compliance with labeling content and format requirements as set forth in 21 CFR 201.66.
- D. **Drug Facts:** Revise as per attached prototype “Drug Facts” labeling.
2. Inform the sponsor that the flags “*Full Prescription Strength*” and “*Full Prescription Strength...Now OTC!*” are not acceptable. These flags must be deleted or revised _____ wherever they appear in the labeling of Zyrtec-D.
 3. Please inform the sponsor that to make more prominent the established names of the active ingredients, dosage forms, and pharmacological categories information for all SKUs, the Agency recommends the following:
 - i. increase the type size and the color contrast lettering of the active ingredients, dosage forms, and pharmacological categories to make more readable.
 - ii. use a more distinguishable graphic feature (e.g., print or color feature) to highlight the dosage strengths (i.e., “5 mg / 120 mg”) of the two active ingredients wherever stated in the labeling.
 4. The flag “New” wherever it appears in the labeling needs to be deleted 6 months after introduction into the OTC marketplace.
 5. Drug Facts annotated specifications are acceptable.
6. **Project Manager:**
- a. The review chemist has indicated in an e-mail dated August 27, 2007 that the blister package is child-resistant.
 - b. This review may be revised based on the completion of the clinical and chemistry reviews. However, this review can be forwarded to the sponsor as our preliminary labeling comments.
 - c. Remind the sponsor of its e-mail dated August 9, 2007, regarding its intention to submit the draft 24-count carton label at a later date for review and comment.
 - d. Please forward the attached “Drug Facts” prototype label to the sponsor.

Cazemiro R. Martin
IDS: Reg. Review Chemist

Concur: Marina Chang, R.Ph.
Team Leader

Enclosure:

- Prototype “Drug Facts” labeling

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 2 Draft Labeling

 Deliberative Process

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/s/

Cazemiro Martin
8/27/2007 12:19:52 PM
INTERDISCIPLINARY

Marina Chang
8/27/2007 01:21:49 PM
INTERDISCIPLINARY



NDA 21-150/S-007

INFORMATION REQUEST LETTER

McNeil Consumer Healthcare
Attention: Robert Kohler
Senior Director, Global Regulatory Affairs
U.S. Agent for Pfizer, Inc.
201 Tabor Road
Morris Plains, NJ 07950

Dear Mr. Kohler:

Please refer to your January 10, 2007 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zyrtec-D 12 Hour (cetirizine HCl 5 mg/pseudoephedrine HCl 120 mg) Tablets.

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

1. Provide baseline stability data as previously requested in our letter dated March 19, 2007. Include comparative moisture permeation data relative to your currently approved packaging configuration.
2. Provide a descriptive engineering drawing of your newly proposed blister configuration designating component materials, dimension, and thickness factors. Include all new related DMF/LOA/supplier control information. Confirm that the blister is in conformance and approved in terms of relevant child resistant packaging provisions.

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

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/s/

Leah Christl
6/22/2007 09:46:07 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 21-150/S-007

McNeil Consumer Healthcare
Attention: Robert Kohler
Senior Director, Global Regulatory Affairs
U.S. Agent for Pfizer, Inc.
201 Tabor Road
Morris Plains, NJ 07950

Dear Mr. Kohler:

Please refer to your January 10, 2007 supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zyrtec-D 12 Hour (cetirizine HCl 5 mg/pseudoephedrine HCl 120 mg) Tablets.

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 March 12, 2007, in accordance with 21 CFR 314.101(a).

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

1. You provided the results of the AERS DataMart database search, but did not include the search criteria used for the search.
2. You did not provide adequate environmental assessment information to include your calculations for your drug substances for their respective Estimation Introductory Concentrations (EIC) at the point of entry into the aquatic environment for each of the three Efficacy Supplements and the new NDA (19-835/S-022, 21-150/S-007, 21-621/S-005 and 22-155).
3. You did not provide an adequate description, controls and supporting information for the blister materials intended to be used for this tablet drug product.
4. You did not identify if you will have a non-child resistant closure.
5. Your NDA submission did not include a debarment certification.

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/s/

Leah Christl
3/19/2007 01:43:16 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-150/S-007

PRIOR APPROVAL SUPPLEMENT

McNeil Consumer Healthcare
Attention: Robert Kohler
Senior Director, Global Regulatory Affairs
U.S. Agent for Pfizer, Inc.
201 Tabor Road
Morris Plains, NJ 07950

Dear Mr. Kohler:

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

Name of Drug Product: Zyrtec-D 12 Hour (cetirizine HCl 5 mg/pseudoephedrine HCl 120 mg) Tablets

NDA Number: 21-150

Supplement number: 007

Review Priority Classification: Standard (S)

Date of supplement: January 10, 2007

Date of receipt: January 11, 2007

This supplemental application proposes a prescription to OTC switch for your product for seasonal allergic rhinitis and perennial allergic rhinitis in adults and children 12 years of age and older.

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 March 12, 2007, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be November 11, 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 application number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

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

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

Sincerely,

{See appended electronic signature page}

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

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Leah Christl
3/9/2007 09:41:29 AM

REQUEST FOR CONSULTATION

(Division/Office): Division of Medication Errors and Technical Support (DMETS)

FROM: Elaine Abraham, RPM
Div. of Nonprescription Clinical Evaluation, WO22, Rm. 5410

DATE February 15, 2007	IND NO.	NDA NO. 21-150 SE6-007	TYPE OF DOCUMENT	DATE OF DOCUMENT January 10, 2007
NAME OF DRUG Zyrtec-D Allergy & Congestion (cetirizine HCl/pseudoephedrine HCl tablets)		PRIORITY CONSIDERATION Med	CLASSIFICATION OF DRUG Antihistamine	DESIRED COMPLETION DATE August 15, 2007

NAME OF FIRM: Pfizer

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|---|
| <input type="checkbox"/> NEW PROTOCOL
<input type="checkbox"/> PROGRESS REPORT
<input type="checkbox"/> NEW CORRESPONDENCE
<input type="checkbox"/> DRUG ADVERTISING
<input type="checkbox"/> ADVERSE REACTION REPORT
<input type="checkbox"/> MANUFACTURING CHANGE/ADDITION
<input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> PRE-NDA MEETING
<input type="checkbox"/> END OF PHASE II MEETING
<input type="checkbox"/> RESUBMISSION
<input type="checkbox"/> SAFETY/EFFICACY
<input type="checkbox"/> PAPER NDA
<input type="checkbox"/> CONTROL SUPPLEMENT | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER
<input type="checkbox"/> FINAL PRINTED LABELING
<input type="checkbox"/> LABELING REVISION
<input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE
<input type="checkbox"/> FORMULATIVE REVIEW
<input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): Trade name review only |
|--|--|---|

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):	<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- | | |
|---|--|
| <input type="checkbox"/> DISSOLUTION
<input type="checkbox"/> BIOAVAILABILITY STUDIES
<input type="checkbox"/> PHASE IV STUDIES | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE
<input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS
<input type="checkbox"/> IN-VIVO WAIVER REQUEST |
|---|--|

IV. DRUG EXPERIENCE

- | | |
|--|---|
| <input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
<input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
<input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below)
<input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
<input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE
<input type="checkbox"/> POISON RISK ANALYSIS |
|--|---|

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> PRECLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS/SPECIAL INSTRUCTIONS:

We are requesting a trade name review of the name "Zyrtec-D Allergy & Congestion". The labeling can be found in the electronic document room (EDR). Please limit your review to consideration of the trade name only. ONP is reviewing all other aspects of the label (principal display panel, Drug Facts content and format etc.). The PDUFA date for this NDA is November 11, 2007. Please contact me at 796-0843 if you have any questions.

SIGNATURE OF REQUESTER See appended electronic signature page}	METHOD OF DELIVERY (Check one) <input type="checkbox"/> MAIL <input type="checkbox"/> HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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/s/

Elaine Abraham
2/16/2007 01:05:02 PM

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 21-150 Supplement # 007 Efficacy Supplement Type SE- SE6

Proprietary Name: Zyrtec-D 12 Hour Tablets
Established Name: cetirizine HCl/pseudoephedrine HCl
Strengths: 5 mg/120 mg

Applicant: Pfizer
Agent for Applicant (if applicable): McNeil

Date of Application: January 10, 2007
Date of Receipt: January 11, 2007
Date clock started after UN:
Date of Filing Meeting: March 7, 2007
Filing Date: March 12, 2007
Action Goal Date (optional): September 11, 2007 User Fee Goal Date: November 11, 2007

Indication(s) requested: Allergic rhinitis

Type of Original NDA: (b)(1) (b)(2)
AND (if applicable)
Type of Supplement: (b)(1) (b)(2)

NOTE:

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

Review Classification: S P
Resubmission after withdrawal? Resubmission after refuse to file?
Chemical Classification: (1,2,3 etc.) 4
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 by contacting the User Fee staff in the Office of Regulatory Policy. 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. 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 any approved (b)(1) or (b)(2) application? YES NO
If yes, explain:

Note: If the drug under review is a 505(b)(2), this issue will be addressed in detail in appendix B.

- 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
If no, explain:
- 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:
- Answer 1, 2, or 3 below (do not include electronic content of labeling as an partial electronic submission).

1. This application is a paper NDA YES
2. This application is an eNDA or combined paper + eNDA YES
This application is: All electronic Combined paper + eNDA
This application is in: NDA format CTD format
Combined NDA and CTD formats

Does the eNDA, follow the guidance?
(<http://www.fda.gov/cder/guidance/2353fml.pdf>) YES NO

If an eNDA, all forms and certifications must be in paper and require a signature.

If combined paper + eNDA, which parts of the application were submitted in electronic format?

Additional comments:

3. This application is an eCTD NDA. YES
If an eCTD NDA, 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"

- Are the required pediatric assessment studies and/or deferral/partial waiver/full waiver of pediatric studies (or request for deferral/partial waiver/full waiver of pediatric studies) included? YES NO
- If the submission contains a request for deferral, partial waiver, or full waiver of studies, does the application contain the certification required under FD&C Act sections 505B(a)(3)(B) and (4)(A) and (B)? YES NO
- Is this submission a partial or complete response to a pediatric Written Request? YES NO

If yes, contact PMHT in the OND-IO

- Financial Disclosure forms included with authorized signature? YES NO
(Forms 3454 and/or 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) YES NO
- PDUFA and Action Goal dates correct in tracking system? YES NO
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.

- Drug name and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.

- List referenced IND numbers: PIND 74,263

- Are the trade, established/proper, and applicant names correct in COMIS? YES NO
If no, have the Document Room make the corrections.

- End-of-Phase 2 Meeting(s) Date(s) _____ NO
If yes, distribute minutes before filing meeting.

- Pre-NDA Meeting(s) Date(s) June 27, 2006 (PIND) NO
If yes, distribute minutes before filing meeting.

- Any SPA agreements? Date(s) _____ NO

If yes, distribute letter and/or relevant minutes before filing meeting.

Project Management

- If Rx, was electronic Content of Labeling submitted in SPL format? YES NO
If no, request in 74-day letter.
- If Rx, for all new NDAs/efficacy supplements submitted on or after 6/30/06: Was the PI submitted in PLR format? YES NO
If no, explain. Was a waiver or deferral requested before the application was received or in the submission? If before, what is the status of the request:
- If Rx, all labeling (PI, PPI, MedGuide, carton and immediate container labels) has been consulted to DDMAC? YES NO
- If Rx, trade name (and all labeling) consulted to OSE/DMETS? YES NO
- If Rx, MedGuide and/or PPI (plus PI) consulted to ODE/DSRCS? N/A YES NO
- Risk Management Plan consulted to OSE/IO? N/A YES NO
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling submitted? NA YES NO

If Rx-to-OTC Switch or OTC application:

- Proprietary name, all OTC labeling/packaging, and current approved PI consulted to OSE/DMETS? YES NO
- If the application was received by a clinical review division, has DNPCE been notified of the OTC switch application? Or, if received by DNPCE, has the clinical review division been notified? 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 EA officer, OPS? YES NO
- Establishment Evaluation Request (EER) submitted to DMPQ? YES NO
- If a parenteral product, consulted to Microbiology Team? YES NO

ATTACHMENT

MEMO OF FILING MEETING

DATE: March 7, 2007

NDA #: 21-150 SE6-007

DRUG NAMES: cetirizine HCl/pseudoephedrine HCl

APPLICANT: Pfizer/McNeil

BACKGROUND: Zyrtec-D (cetirizine HCl 5 mg/pseudoephedrine HCl 120 mg) was approved as a prescription product for SAR and PAR (> 12 yrs) on August 10, 2001. This supplement is for the Rx-to-OTC switch of Zyrtec-D tablets. Pfizer is the innovator of cetirizine. After approval, the product will be marketed by McNeil. The Division of Nonprescription Clinical Evaluation is the lead division for this NDA and the Division of Pulmonary and Allergy Products is reviewing clinical efficacy.

(Provide a brief background of the drug, (e.g., molecular entity 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, Joel Schiffenbauer, Daiva Shetty, Marina Chang, Sally Seymour, Tayo Fadiran, Jim Vidra in addition to assigned reviewers

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

<u>Discipline/Organization</u>	<u>Reviewer</u>
Medical:	Susan Limb
Secondary Medical:	Steve Osborne
Statistical:	
Pharmacology:	Wafa Harrouk
Statistical Pharmacology:	
Chemistry:	Stuart Zimmerman
Environmental Assessment (if needed):	
Biopharmaceutical:	Partha Roy
Microbiology, sterility:	
Microbiology, clinical (for antimicrobial products only):	
DSI:	Tejashri Purohit-Sheth (unable to attend)
OPS:	
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 audit(s) needed? YES NO
If no, explain:
- 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. study site audits(s) needed? YES NO

PHARMACOLOGY/TOX N/A FILE REFUSE TO FILE

• GLP audit needed? YES NO

CHEMISTRY FILE REFUSE TO FILE

• Establishment(s) ready for inspection? YES NO

• Sterile product? YES NO

 If yes, was microbiology consulted for validation of sterilization? 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): Numerous including labeling - hives and allergy on same container, chemistry - environmental assessment

ACTION ITEMS:

1. Ensure that the review and chemical classification codes, as well as any other pertinent classification codes (e.g., orphan, OTC) are correctly entered into COMIS.
2. If RTF, notify everybody who already received a consult request of RTF action. Cancel the EER.
3. 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.
4. If filed, complete the Pediatric Page at this time. (If paper version, enter into DFS.)

5. Convey document filing issues/no filing issues to applicant by Day 74.

Elaine Abraham
Regulatory Project Manager

Appears This Way
On Original

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

/s/

Elaine Abraham
5/1/2007 11:57:35 AM
CSO

ACTION PACKAGE CHECKLIST

Application Information		
BLA # NDA # 21-150	BLA STN# NDA Supplement # 007	If NDA, Efficacy Supplement Type SE6
Proprietary Name: Zyrtec-D Established Name: cetirizine HCl/pseudoephedrine HCl Dosage Form: ER tablet		Applicant: McNeil
RPM: Elaine Abraham		Division: DNCE Phone # (301) 796-0843
<p>NDA Application Type: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>Efficacy Supplement: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p>		<p>505(b)(2) NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p><input type="checkbox"/> If no listed drug, check here and explain:</p> <p>Review and confirm the information previously provided in Appendix B to the Regulatory Filing Review. Use this Checklist to update any information (including patent certification information) that is no longer correct.</p> <p><input type="checkbox"/> Confirmed <input type="checkbox"/> Corrected</p> <p>Date:</p>
❖ User Fee Goal Date		11/11/07
❖ Action Goal Date (if different)		
❖ Actions		
• Proposed action		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA <input type="checkbox"/> CR
• Previous actions (specify type and date for each action taken)		<input checked="" type="checkbox"/> None
❖ 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

❖ Application Characteristics	
Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): 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 NDAs and NDA Supplements: <input checked="" type="checkbox"/> OTC drug Other: Other comments:	
❖ Application Integrity Policy (AIP)	
<ul style="list-style-type: none"> Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> This application is on the AIP <ul style="list-style-type: none"> Exception for review (<i>file Center Director's memo in Administrative Documents section</i>) OC clearance for approval (<i>file communication in Administrative Documents section</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> Not an AP action
❖ Public communications (approvals only)	
<ul style="list-style-type: none"> Office of Executive Programs (OEP) liaison has been notified of action 	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> Press Office notified of action 	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> Indicate what types (if any) of information dissemination are anticipated 	<input type="checkbox"/> None <input checked="" type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

❖ Exclusivity	
<ul style="list-style-type: none"> • NDAs: Exclusivity Summary (approvals only) (<i>file Summary in Administrative Documents section</i>) 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> • Is approval of this application blocked by any type of exclusivity? <ul style="list-style-type: none"> • NDAs/BLAs: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of “same drug” for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i> • NDAs: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? (<i>Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.</i>) • NDAs: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? (<i>Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.</i>) • NDAs: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? (<i>Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.</i>) 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # and date exclusivity expires: <input type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA # and date exclusivity expires: <input type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA # and date exclusivity expires:
❖ Patent Information (NDAs and NDA supplements only)	
<ul style="list-style-type: none"> • Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> • Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. • [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii) <input type="checkbox"/> No paragraph III certification Date patent will expire
<ul style="list-style-type: none"> • [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). (<i>If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews).</i>) • [505(b)(2) applications] For each paragraph IV certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation. Answer the following questions for each paragraph IV certification: (1) Have 45 days passed since the patent owner’s receipt of the applicant’s 	<input type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> Verified <input type="checkbox"/> Yes <input type="checkbox"/> No

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>	
Summary Reviews	
❖ Summary Reviews (e.g., Office Director, Division Director) (indicate date for each review)	11/7/07, 11/8/07 (2)
❖ BLA approvals only: Licensing Action Recommendation Memo (LARM) (indicate date)	
Labeling	
❖ Package Insert	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) • Original applicant-proposed labeling • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	1/10/07 10/30/07
❖ Patient Package Insert	
<ul style="list-style-type: none"> • Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling) • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) • Original applicant-proposed labeling • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	
❖ Medication Guide	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) • Original applicant-proposed labeling • Other relevant labeling (e.g., most recent 3 in class, class labeling) 	
❖ Labels (full color carton and immediate-container labels)	
<ul style="list-style-type: none"> • Most-recent division-proposed labels (only if generated after latest applicant submission) • Most recent applicant-proposed labeling 	11/6/07
❖ Labeling reviews and minutes of any labeling meetings (indicate dates of reviews and meetings)	<input checked="" type="checkbox"/> DMETS 11/7/07 <input type="checkbox"/> DSRCS <input type="checkbox"/> DDMAC <input type="checkbox"/> SEALD <input checked="" type="checkbox"/> Other reviews 8/27/07, 10/24/07, 11/08/07 <input type="checkbox"/> Memos of Mtgs

Administrative Documents	
❖ Administrative Reviews (RPM Filing Review/Memo of Filing Meeting; ADRA) (indicate date of each review)	5/1/07
❖ NDA and NDA supplement approvals only: Exclusivity Summary (signed by Division Director)	<input checked="" type="checkbox"/> Included
❖ AIP-related documents <ul style="list-style-type: none"> Center Director's Exception for Review memo If AP: OC clearance for approval 	
❖ Pediatric Page (all actions)	<input checked="" type="checkbox"/> Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent. (Include certification.)	<input checked="" type="checkbox"/> Verified, statement is acceptable
❖ Postmarketing Commitment Studies <ul style="list-style-type: none"> Outgoing Agency request for post-marketing commitments (if located elsewhere in package, state where located) Incoming submission documenting commitment 	<input checked="" type="checkbox"/> None
❖ Outgoing correspondence (letters including previous action letters, emails, faxes, telecons)	6/22/07, 8/29/07, 10/25/07
❖ Internal memoranda, telecons, email, etc.	
❖ Minutes of Meetings <ul style="list-style-type: none"> Pre-Approval Safety Conference (indicate date; approvals only) Pre-NDA/BLA meeting (indicate date) EOP2 meeting (indicate date) Other (e.g., EOP2a, CMC pilot programs) 	<input checked="" type="checkbox"/> No mtg <input type="checkbox"/> No mtg
❖ Advisory Committee Meeting <ul style="list-style-type: none"> Date of Meeting 48-hour alert or minutes, if available 	<input checked="" type="checkbox"/> No AC meeting
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	
CMC/Product Quality Information	
❖ CMC/Product review(s) (indicate date for each review)	9/5/07
❖ Reviews by other disciplines/divisions/Centers requested by CMC/product reviewer (indicate date for each review)	<input checked="" type="checkbox"/> None
❖ BLAs: Product subject to lot release (APs only)	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Environmental Assessment (check one) (original and supplemental applications) <ul style="list-style-type: none"> <input type="checkbox"/> Categorical Exclusion (indicate review date)(all original applications and all efficacy supplements that could increase the patient population) <input type="checkbox"/> Review & FONSI (indicate date of review) <input type="checkbox"/> Review & Environmental Impact Statement (indicate date of each review) 	9/5/07
❖ NDAs: Microbiology reviews (sterility & apyrogenicity) (indicate date of each review)	<input type="checkbox"/> Not a parenteral product
❖ Facilities Review/Inspection <ul style="list-style-type: none"> NDAs: Facilities inspections (include EER printout) 	Date completed: 7/13/07 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation

❖ BLAs: Facility-Related Documents <ul style="list-style-type: none"> • Facility review (<i>indicate date(s)</i>) • Compliance Status Check (approvals only, both original and supplemental applications) (<i>indicate date completed, must be within 60 days prior to AP</i>) 	<input type="checkbox"/> Requested <input type="checkbox"/> Accepted <input type="checkbox"/> Hold
❖ NDAs: Methods Validation	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed
Nonclinical Information	
❖ Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	
❖ Nonclinical inspection review Summary (DSI)	<input type="checkbox"/> None requested
Clinical Information	
❖ Clinical review(s) (<i>indicate date for each review</i>)	9/7/07, 9/10/07
❖ Financial Disclosure reviews(s) or location/date if addressed in another review	incl
❖ Clinical consult reviews from other review disciplines/divisions/Centers (<i>indicate date of each review</i>)	<input type="checkbox"/> None
❖ Microbiology (efficacy) reviews(s) (<i>indicate date of each review</i>)	<input type="checkbox"/> Not needed
❖ Safety Update review(s) (<i>indicate location/date if incorporated into another review</i>)	9/7/07
❖ 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 type="checkbox"/> Not needed
❖ DSI Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input checked="" type="checkbox"/> None requested
• Clinical Studies	
• Bioequivalence Studies	
• Clin Pharm Studies	
❖ Statistical Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None

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.

Store: PDUFA CoverSheet

Page 1 of 1

Form Approved: OMB No. 0910 - 0297 Expiration Date: December 31, 2006 See instructions for OMB Statement.		
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 PFIZER INC Hans Knapp 201 Tabor Road Morris Plains NJ 07950 US		4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER 21-150
2. TELEPHONE NUMBER 973-385 7250		5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? <input checked="" type="checkbox"/> YES <input type="checkbox"/> 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: <input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:
3. PRODUCT NAME Zyrtec-D 12 Hour Extended-Release Tablets (Cetirizine HCl/Pseudoephedrine HCl)		6. USER FEE I.D. NUMBER PD3006966
7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION. <input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory) <input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE <input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act <input type="checkbox"/> 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? <input type="checkbox"/> YES <input checked="" type="checkbox"/> 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 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. Food and Drug Administration CDER, HFD-94 CBER, HFM-99 12420 Parklawn Drive, Room 3046 1401 Rockville Pike Rockville, MD 20852 Rockville, MD 20852-1448		
SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE 		TITLE SA DIRECTOR REGULATORY AFFAIRS
		DATE 1/9/07
9. USER FEE PAYMENT AMOUNT FOR THIS APPLICATION \$448,100.00		
Form FDA 3397 (12/03)		

Close Print Cover sheet