# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

**21-909**

# ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Department of Health and Human Services
Food and Drug Administration

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

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

Form Approved: OMB No. 0910-0513
Expiration Date: 07/31/06
*See OMB Statement on Page 3.*

NDA NUMBER
21909

NAME OF APPLICANT / NDA HOLDER
Sanofi-Aventis U.S. LLC

***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)
ALLEGRA ODT

| ACTIVE INGREDIENT(S) | STRENGTH(S) |
|---|---|
| Fexofenadine hydrochloride | 30mg |

DOSAGE FORM
Orally Disintegrating Tablet

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

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

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

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

## 1. GENERAL

| a. United States Patent Number | b. Issue Date of Patent | c. Expiration Date of Patent |
|---|---|---|
| 5,178,878 | 1/12/1993 | 1/12/2010 |

d. Name of Patent Owner
Cima Labs, Inc.

Address *(of Patent Owner)*
10000 Valley View Road

City/State
Eden Prairie, Minnesota

| ZIP Code | FAX Number *(if available)* |
|---|---|
| 55344 | 763-488-4770 |
| **Telephone Number** | **E-Mail Address *(if available)*** |
| 763-488-4790 | tom.rendos@cimalabs.com |

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

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

City/State

| ZIP Code | FAX Number *(if available)* |
|---|---|
| **Telephone Number** | **E-Mail Address *(if available)*** |

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

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

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

## 2. Drug Substance (Active Ingredient)

| | | | |
|---|---|---|---|
| **2.1** | Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? | ☐ Yes | ☒ No |
| **2.2** | Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? | ☐ Yes | ☒ No |
| **2.3** | If the answer to question **2.2** is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). | ☐ Yes | ☐ No |
| **2.4** | Specify the polymorphic form(s) claimed by the patent for which you have the test results described in **2.3**. | | |
| 2.5 | Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) | ☐ Yes | ☒ No |
| **2.6** | Does the patent claim only an intermediate? | ☐ Yes | ☒ No |
| **2.7** | If the patent referenced in **2.1** is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) | ☐ Yes | ☐ No |

## 3. Drug Product (Composition/Formulation)

| | | | |
|---|---|---|---|
| | 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)*<br>Claims 12 and 13 | 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 Use: *(Submit indication or method of use information as identified specifically in the approved labeling.)* | | |

Appears This Way
On Original

| | |
|---|---|
| "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. | Patent Claims generally: A method of administering at least one systemically distributable pharmaceutical ingredient to a human patient comprising the steps of: 1) providing a tablet as described in NDA 21909 and 2) placing said tablet in the mouth of a patient<br><br>Use: ALLEGRA (fexofenadine HCl) ODT 30mg is indicated for the relief of symptoms associated with seasonal allergic rhinitis and for the treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in children 6 to 11 years of age.<br><br>The proposed INDICATIONS AND USAGE are as follows:<br>Seasonal Allergic Rhinitis<br>ALLEGRA is indicated for the relief of symptoms associated with seasonal allergic rhinitis in adults and children 2 years of age and older. Symptoms treated effectively were sneezing, rhinorrhea, itchy nose/palate/throat, itchy/watery/red eyes.<br><br>Chronic Idiopathic Urticaria<br>ALLEGRA is indicated for treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 6 months of age and older. It significantly reduces pruritus and the number of wheals. |

**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 |
|---|---|
| Charlotte L. Barney | 9/11/06 |

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

**Check applicable box and provide information below.**

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

| | |
|---|---|
| Name<br>Charlotte L. Barney<br>Associate General Counsel, US Patent Litigation | |
| Address<br>Sanofi Aventis Pharmaceuticals<br>1041 Route 202-206<br>P.O. Box 6800 | City/State<br>Bridgewater, New Jersey |
| ZIP Code<br>08807-0800 | Telephone Number<br>908-231-4551 |
| FAX Number *(if available)*<br>908-231-2840 | E-Mail Address *(if available)*<br>charlotte.barney@sanofi-aventis.com |

Department of Health and Human Services
Food and Drug Administration

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| ACTIVE INGREDIENT(S) | STRENGTH(S) |
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## 1. GENERAL

| a. United States Patent Number | b. Issue Date of Patent | c. Expiration Date of Patent |
|---|---|---|
| 5,578,610 | 11/26/1996 | 11/26/2013 |

d. Name of Patent Owner
AMR Technology

Address *(of Patent Owner)*
5429 Main Street
P.O. Box 2587

City/State
Manchester Center, Vermont

| ZIP Code | FAX Number *(if available)* |
|---|---|
| 05255-2587 | 802-362-3264 |
| **Telephone Number** | **E-Mail Address *(if available)*** |
| 802-362-5158 | davidw@albmolecular.com |

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

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

City/State

| ZIP Code | FAX Number *(if available)* |
|---|---|
| **Telephone Number** | **E-Mail Address *(if available)*** |

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

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

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

## 2. Drug Substance (Active Ingredient)

| | | | |
|---|---|---|---|
| 2.1 | Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? | ☒ Yes | ☐ No |
| 2.2 | Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? | ☐ Yes | ☒ No |
| 2.3 | If the answer to question **2.2** is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). | ☐ Yes | ☐ No |
| 2.4 | Specify the polymorphic form(s) claimed by the patent for which you have the test results described in **2.3**. | | |
| 2.5 | Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) | ☐ Yes | ☒ No |
| 2.6 | Does the patent claim only an intermediate? | ☐ Yes | ☒ No |
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## 3. Drug Product (Composition/Formulation)

| | | | |
|---|---|---|---|
| | Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? | ☒ Yes | ☐ No |
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## 4. Method of Use

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| | | | |
|---|---|---|---|
| 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)*: Claim 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.)*

Patent Claims generally: A method of treating allergic reactions in a patient.

Use: ALLEGRA (fexofenadine HCl) ODT 30mg is indicated for the relief of symptoms associated with seasonal allergic rhinitis and for the treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in children 6 to 11 years of age.

The proposed INDICATIONS AND USAGE are as follows:

Seasonal Allergic Rhinitis: ALLEGRA ODT is indicated for the relief of symptoms associated with seasonal allergic rhinitis in children 6 to 11 years of age. Symptoms treated effectively were sneezing, rhinorrhea, itchy nose/palate/throat, itchy/watery/red eyes.

Chronic Idiopathic Urticaria: ALLEGRA ODT is indicated for treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in children 6 to 11 years of age. It significantly reduces pruritus and the number of wheals.

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☐ Yes

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|---|---|
| Charlotte L Barney | 9/11/06 |

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**Check applicable box and provide information below.**

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

| | |
|---|---|
| Name<br>Charlotte L. Barney<br>Associate General Counsel, US Patent Litigation | |
| Address<br>Sanofi Aventis Pharmaceuticals Inc.<br>1041 Route 202-206<br>P.O. Box 6800 | City/State<br>Bridgewater, New Jersey |
| ZIP Code<br>08807-0800 | Telephone Number<br>908-231-4551 |
| FAX Number *(if available)*<br>908-231-2840 | E-Mail Address *(if available)*<br>charlotte.barney@sanofi-aventis.com |

Notes to Form FDA 3542a for U.S. Patent 5,578,610 for NDA 21909 (Allegra ODT)

Note to Question 2.2. U.S. Patent 5,578,610 claims one of the active ingredients of the drug product [Allegra ODT] (fexofenadine) as a substantially pure compound, and these claims are not limited to specific polymorphic forms. However, the patent does not specifically claim any particular polymorph of the active ingredient fexofenadine, and therefore the answer to Question 2.2 is "no".

Department of Health and Human Services
Food and Drug Administration

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DOSAGE FORM
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## 1. GENERAL

| a. United States Patent Number | b. Issue Date of Patent | c. Expiration Date of Patent |
|---|---|---|
| 5,738,872 | 4/14/1998 | 2/28/2015 |

d. Name of Patent Owner
Hoechst Marion Roussel, Inc. (now known as Sanofi-Aventis U.S. Inc. )

Address *(of Patent Owner)*
300 Somerset Corporate Boulevard

City/State
Bridgewater, New Jersey

| ZIP Code | FAX Number *(if available)* |
|---|---|
| 08807 | 908-243-7083 |
| **Telephone Number** | **E-Mail Address *(if available)*** |
| 908-243-6000 | |

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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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 |
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## 3. Drug Product (Composition/Formulation)

| | | | |
|---|---|---|---|
| | 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.)* | |

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| ☐ Patent Owner | ☒ Patent Owner's Attorney, Agent (Representative) or Other Authorized Official |

| | |
|---|---|
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NAME OF APPLICANT / NDA HOLDER
Sanofi-Aventis U.S. LLC

***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)
ALLEGRA ODT

| ACTIVE INGREDIENT(S) | STRENGTH(S) |
|---|---|
| Fexofenadine hydrochloride | 30mg |

DOSAGE FORM
Orally Disintegrating Tablet

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

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

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

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

## 1. GENERAL

| a. United States Patent Number | b. Issue Date of Patent | c. Expiration Date of Patent |
|---|---|---|
| 6,037,353 | 3/14/2000 | 3/14/2017 |

| d. Name of Patent Owner | Address *(of Patent Owner)* | |
|---|---|---|
| Merrell Pharmaceuticals, Inc. | 3711 Kennett Pike, Suite 200 | |
| | City/State: Greenville, DE | |
| | ZIP Code: 19807 | FAX Number *(if available)*: 302-777-7665 |
| | Telephone Number: 302-777-7222 | E-Mail Address *(if available)*: |

| e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States) | Address *(of agent or representative named in 1.e.)* | |
|---|---|---|
| | City/State | |
| | ZIP Code | FAX Number *(if available)* |
| | Telephone Number | E-Mail Address *(if available)* |

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

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


PSC Media Arts (301) 443-1090 EF

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

## 2. Drug Substance (Active Ingredient)

| | | | |
|---|---|---|---|
| 2.1 | Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? | ☐ Yes | ☒ No |
| 2.2 | Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? | ☐ Yes | ☒ No |
| 2.3 | If the answer to question **2.2** is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). | ☐ Yes | ☐ No |
| 2.4 | Specify the polymorphic form(s) claimed by the patent for which you have the test results described in **2.3**. | | |
| 2.5 | Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) | ☐ Yes | ☒ No |
| 2.6 | Does the patent claim only an intermediate? | ☐ Yes | ☒ No |
| 2.7 | If the patent referenced in **2.1** is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) | ☐ Yes | ☐ No |

## 3. Drug Product (Composition/Formulation)

| | | | |
|---|---|---|---|
| | 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)*: Claims 1, 2, 3, 4, 5

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.)*

Patent Claims generally: A method of treating a histamine-mediated condition in a patient having impaired liver function due to disease or due to administration of a concomitant drug which inhibits normal liver metabolic function while avoiding cardiac events associated with administration of terfenadine.

Use: ALLEGRA (fexofenadine HCl) ODT 30mg is indicated for the relief of symptoms associated with seasonal allergic rhinitis and for the treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in children 6 to 11 years of age.

Proposed Labeling: 1) INDICATIONS AND USAGE; 2) a relevant section from proposed PRECAUTIONS (Drug Interactions), and 3) a relevant section from proposed CLINICAL PHARMACOLOGY (Special Populations--Hepatically Impaired) are provided in the "Note to Form FDA 3542a for U.S. Patent 6,037,353 submitted herewith for NDA 21909 (Allegra ODT); Note to Question 4.2(a).

**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 |
|---|---|
| Charlotte L Barney | 9/11/06 |

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

**Check applicable box and provide information below.**

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

Name
Charlotte L. Barney
Associate General Counsel, US Patent Litigation

| Address | City/State |
|---|---|
| Sanofi Aventis Pharmaceuticals Inc.<br>1041 Route 202-206<br>P.O. Box 6800 | Bridgewater, New Jersey |
| ZIP Code<br>08807-0800 | Telephone Number<br>908-231-4551 |
| FAX Number *(if available)*<br>908-231-2840 | E-Mail Address *(if available)*<br>charlotte.barney@sanofi-aventis.com |

Note to Form FDA 3542a for U.S. Patent 6,037,353 submitted herewith for sNDA 21909 (Allegra ODT)

Note to Question 4.2(a): The proposed 1) **INDICATIONS AND USAGE,** 2) a relevant section from proposed **PRECAUTIONS** (Drug Interactions), and 3) a relevant section from proposed **CLINICAL PHARMACOLOGY** (Special Populations—Hepatically Impaired) are as follows:

## INDICATIONS AND USAGE

**Seasonal Allergic Rhinitis**
ALLEGRA is indicated for the relief of symptoms associated with seasonal allergic rhinitis in adults and children 2 years of age and older. Symptoms treated effectively were sneezing, rhinorrhea, itchy nose/palate/throat, itchy/watery/red eyes.

**Chronic Idiopathic Urticaria**
ALLEGRA is indicated for treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 6 months of age and older. It significantly reduces pruritus and the number of wheals.

## PRECAUTIONS

**Drug Interactions**

Fexofenadine has been shown to exhibit minimal (ca. 5%) metabolism. However, co-administration of fexofenadine hydrochloride with either ketoconazole or erythromycin led to increased plasma concentrations of fexofenadine hydrochloride in healthy adult subjects. Fexofenadine had no effect on the pharmacokinetics of either erythromycin and ketoconazole. In 2 separate studies in healthy adult subjects, fexofenadine hydrochloride 120 mg twice daily (240 mg total daily dose) was co-administered with either erythromycin 500 mg every 8 hours or ketoconazole 400 mg once daily under steady state conditions to healthy adult subjects (n=24, each study). No differences in adverse events or QTc interval were observed when subjects were administered fexofenadine hydrochloride alone or in combination with either erythromycin or ketoconazole. The findings of these studies are summarized in the following table:

**Effects on steady-state fexofenadine pharmacokinetics after 7 days of co-administration with fexofenadine hydrochloride 120mg every 12 hours in healthy adult subjects (n=24)**

| *Concomitant Drug* | $C_{maxSS}$ *(Peak plasma concentration)* | $AUC_{ss(0\text{-}12h)}$ *(Extent of systemic exposure)* |
|---|---|---|
| Erythromycin (500mg every 8 hours) | +82% | +109% |
| Ketoconazole (400mg once daily) | +135% | +164% |

The changes in plasma levels were within the range of plasma levels achieved in adequate and well-controlled clinical trials.

The mechanism of these interactions has been evaluated in *in vitro*, *in situ* and *in vivo* animal models. These studies indicate that ketoconazole or erythromycin co-administration enhances fexofenadine gastrointestinal absorption. The observed increase in the bioavailability of fexofenadine may be due to transport-related effects, such a p-glycoprotein. In vivo animal studies also suggest that in addition to enhancing absorption, ketoconazole decreases fexofenadine gastrointestinal secretion, while erythromycin may also decrease biliary excretion.

## CLINICAL PHARMACOLOGY

**Special Populations**
Pharmacokinetics in renally and hepatically impaired subjects and geriatric subjects, obtained after a single does of 80 mg fexofenadine hydrochloride, were compared to those from healthy subjects in a separate study of similar design.

**Hepatic Impairment.** The pharmacokinetics of fexofenadine hydrochloride in subjects with hepatic disease did not differ substantially from that observed in healthy subjects.

Department of Health and Human Services
Food and Drug Administration

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

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

Form Approved: OMB No. 0910-0513
Expiration Date: 07/31/06
*See OMB Statement on Page 3.*

NDA NUMBER
21909

NAME OF APPLICANT / NDA HOLDER
Sanofi-Aventis U.S. LLC

***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)
ALLEGRA ODT

| ACTIVE INGREDIENT(S) | STRENGTH(S) |
|---|---|
| Fexofenadine hydrochloride | 30mg |

DOSAGE FORM
Orally Disintegrating Tablet

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

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

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

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

## 1. GENERAL

| a. United States Patent Number | b. Issue Date of Patent | c. Expiration Date of Patent |
|---|---|---|
| 6,187,791 | 2/13/2001 | 5/11/2012 |

d. Name of Patent Owner
Carderm Capital L.P.

Address *(of Patent Owner)*
c/o Westbroke Ltd.
Richmond House Par-La-Ville Road
P.O. Box HM 1022

City/State
HMR DX Hamilton, Bermuda

| ZIP Code | FAX Number *(if available)* |
|---|---|
| | 441-292-0865 |
| **Telephone Number** | **E-Mail Address *(if available)*** |
| 441-292-3434 | |

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)

Charlotte L. Barney
Associate General Counsel, US Patent Litigation

Address *(of agent or representative named in 1.e.)*
Sanofi-Aventis U.S. Inc.
1041 Route 202-206
P.O. Box 6800

City/State
Bridgewater, New Jersey

| ZIP Code | FAX Number *(if available)* |
|---|---|
| 08807-0800 | 908-231-2840 |
| **Telephone Number** | **E-Mail Address *(if available)*** |
| 908-231-4551 | charlotte.barney@sanofi-aventis.com |

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

| | |
|---|---|
| 3. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? | ☐ Yes ☐ No |

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

## 2. Drug Substance (Active Ingredient)

| | | | |
|---|---|---|---|
| **2.1** | Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? | ☐ Yes | ☒ No |
| **2.2** | Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? | ☐ Yes | ☒ No |
| **2.3** | If the answer to question **2.2** is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). | ☐ Yes | ☐ No |
| **2.4** | Specify the polymorphic form(s) claimed by the patent for which you have the test results described in **2.3**. | | |
| **2.5** | Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) | ☐ Yes | ☒ No |
| **2.6** | Does the patent claim only an intermediate? | ☐ Yes | ☒ No |
| **2.7** | If the patent referenced in **2.1** is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) | ☐ Yes | ☐ No |

## 3. Drug Product (Composition/Formulation)

| | | | |
|---|---|---|---|
| | 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)*: Claims 1, 2, 5, 6, 7, 8, 9

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.)*

Patent Claims generally: A method of treating a histaminic or histamine-related condition or disease, or providing an antihistaminic effect to 1) patients susceptible to possible cardiac events associated with the administration of terfenadine; 2) humans while avoiding the concomitant liability of cardiac arrythmias associated with the administration of terfenadine; or 3) patients susceptible to QT prolongation and/or ventricular tachycardia when using terfenadine.

Use: ALLEGRA (fexofenadine HCl) ODT 30mg is indicated for the relief of symptmos associated with seasonal allergic rhinitis and for the treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in children 6 to 11 years of age.

Proposed Labeling: 1) INDICATIONS AND USAGE; 2) a relevant section from proposed PRECAUTIONS (Drug Interactions), and 3) a relevant section from proposed CLINICAL PHARMACOLOGY (Special Populations--Hepatically Impaired) are provided in the "Note to Form FDA 3542a for U.S. Patent 6,187,791 submitted herewith for NDA 21909 (Allegra ODT); Note to Question 4.2(a)

**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)*

Charlotte L. Barney

Date Signed: 9/11/06

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

**Check applicable box and provide information below.**

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

Name
Charlotte L. Barney
Associate General Counsel, US Patent Litigation

| | |
|---|---|
| Address<br>Sanofi Aventis Pharmaceuticals Inc.<br>1041 Route 202-206<br>P.O. Box 6800 | City/State<br>Bridgewater, New Jersey |
| ZIP Code<br>08807-0800 | Telephone Number<br>908-231-4551 |
| FAX Number *(if available)*<br>908-231-2840 | E-Mail Address *(if available)*<br>charlotte.barney@sanofi-aventis.com |

Note to Form FDA 3542a for U.S. Patent 6,187,791 submitted herewith for NDA 21909 (Allegra-ODT)

Note to Question 4.2(a): The proposed 1) **INDICATIONS AND USAGE,** 2) a relevant section from proposed **PRECAUTIONS** (Drug Interactions), and 3) a relevant section from proposed **CLINICAL PHARMACOLOGY** (Special Populations—Hepatically Impaired) are as follows:

## INDICATIONS AND USAGE

### Seasonal Allergic Rhinitis

ALLEGRA is indicated for the relief of symptoms associated with seasonal allergic rhinitis in adults and children 2 years of age and older. Symptoms treated effectively were sneezing, rhinorrhea, itchy nose/palate/throat, itchy/watery/red eyes.

### Chronic Idiopathic Urticaria

ALLEGRA is indicated for treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 6 months of age and older. It significantly reduces pruritus and the number of wheals.

## PRECAUTIONS

### Drug Interactions

Fexofenadine has been shown to exhibit minimal (ca. 5%) metabolism. However, co-administration of fexofenadine hydrochloride with either ketoconazole or erythromycin led to increased plasma concentrations of fexofenadine hydrochloride in healthy adult subjects. Fexofenadine had no effect on the pharmacokinetics of either erythromycin and ketoconazole. In 2 separate studies in healthy adult subjects, fexofenadine hydrochloride 120 mg twice daily (240 mg total daily dose) was co-administered with either erythromycin 500 mg every 8 hours or ketoconazole 400 mg once daily under steady state conditions to healthy adult subjects (n=24, each study). No differences in adverse events or QTc interval were observed when subjects were administered fexofenadine hydrochloride alone or in combination with either erythromycin or ketoconazole. The findings of these studies are summarized in the following table:

**Effects on steady-state fexofenadine pharmacokinetics after 7 days of co-administration with fexofenadine hydrochloride 120mg every 12 hours in healthy adult subjects (n=24)**

| *Concomitant Drug* | $C_{maxSS}$ *(Peak plasma concentration)* | $AUC_{ss(0\text{-}12h)}$ *(Extent of systemic exposure)* |
|---|---|---|
| Erythromycin (500mg every 8 hours) | +82% | +109% |
| Ketoconazole (400mg once daily) | +135% | +164% |

The changes in plasma levels were within the range of plasma levels achieved in adequate and well-controlled clinical trials.

The mechanism of these interactions has been evaluated in *in vitro*, *in situ* and *in vivo* animal models. These studies indicate that ketoconazole or erythromycin co-administration enhances fexofenadine gastrointestinal absorption. The observed increase in the bioavailability of fexofenadine may be due to transport-related effects, such a p-glycoprotein. In vivo animal studies also suggest that in addition to enhancing absorption, ketoconazole decreases fexofenadine gastrointestinal secretion, while erythromycin may also decrease biliary excretion.

## CLINICAL PHARMACOLOGY

**Special Populations**
Pharmacokinetics in renally and hepatically impaired subjects and geriatric subjects, obtained after a single does of 80 mg fexofenadine hydrochloride, were compared to those from healthy subjects in a separate study of similar design.

**Hepatic Impairment.** The pharmacokinetics of fexofenadine hydrochloride in subjects with hepatic disease did not differ substantially from that observed in healthy subjects.

Department of Health and Human Services
Food and Drug Administration

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

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

Form Approved: OMB No. 0910-0513
Expiration Date: 07/31/06
*See OMB Statement on Page 3.*

NDA NUMBER
21909

NAME OF APPLICANT / NDA HOLDER
Sanofi-Aventis U.S. LLC

***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)
ALLEGRA ODT

| ACTIVE INGREDIENT(S) | STRENGTH(S) |
|---|---|
| Fexofenadine hydrochloride | 30mg |

DOSAGE FORM
Orally Disintegrating Tablet

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

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

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

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

## 1. GENERAL

| a. United States Patent Number | b. Issue Date of Patent | c. Expiration Date of Patent |
|---|---|---|
| 6,399,632 | 6/4/2002 | 5/11/2012 |

| d. Name of Patent Owner | Address *(of Patent Owner)* | |
|---|---|---|
| Carderm Capital L.P. | c/o Westbroke Ltd.<br>Richmond House Par-La-Ville Road | |
| | City/State<br>HMR DX Hamilton, Bermuda | |
| | ZIP Code | FAX Number *(if available)*<br>441-292-0865 |
| | Telephone Number<br>441-292-3434 | 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.)* | |
|---|---|---|
| Charlotte L. Barney<br>Associate General Counsel, US Patent Litigation | Sanofi-Aventis U.S. Inc.<br>1041 Route 202-206<br>P.O. Box 6800 | |
| | City/State<br>Bridgewater, New Jersey | |
| | ZIP Code<br>08807-0800 | FAX Number *(if available)*<br>908-231-2840 |
| | Telephone Number<br>908-231-4551 | E-Mail Address *(if available)*<br>charlotte.barney@sanofi-aventis.com |

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

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

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

## 2. Drug Substance (Active Ingredient)

| | | | |
|---|---|---|---|
| 2.1 | Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? | ☐ Yes | ☒ No |
| 2.2 | Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? | ☐ Yes | ☒ No |
| 2.3 | If the answer to question **2.2** is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). | ☐ Yes | ☐ No |
| 2.4 | Specify the polymorphic form(s) claimed by the patent for which you have the test results described in **2.3**. | | |
| 2.5 | Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) | ☐ Yes | ☒ No |
| 2.6 | Does the patent claim only an intermediate? | ☐ Yes | ☒ No |
| 2.7 | If the patent referenced in **2.1** is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) | ☐ Yes | ☐ No |

## 3. Drug Product (Composition/Formulation)

| | | | |
|---|---|---|---|
| | 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? | | |
|---|---|---|---|
| Claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 | | ☒ Yes | ☐ No |

**4.2a** If the answer to **4.2** is Use: *(Submit indication or method of use information as identified specifically in the approved labeling.)*

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| | |
|---|---|
| "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. | Patent Claims generally: A method of treating a histamine-mediated condition or providing/obtaining an antihistaminic effect in a 1) a patient in whom terfenadine is not metabolized at the normal rate to the terfenadine acid metabolite, while avoiding the concomitant liability of cardiac arrythmias associated with the administration of terfenadine; 2) a patient in whom terfenadine is not metabolized at the normal rate to the terfenadine acid metabolite; 3) a patient in whom terfenadine is not metabolized at the normal rate to terfenadine acid metabolite and who is subject to QT prolongation and/or ventricular tachycardia when using terfenadine; or 4) a human who also received a product which inhibits terfenadine metabolism.<br><br>Use: ALLEGRA (fexofenadine HCl) ODT 30mg is indicated for the relief of symptoms associated with seasonal allergic rhinitis and for the treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in children 6 to 11 years of age.<br><br>Proposed Labeling: 1) INDICATIONS AND USAGE; 2) a relevant section from proposed PRECAUTIONS (Drug Interactions), and 3) a relevant section from proposed CLINICAL PHARMACOLOGY (Special Populations--Hepatically Impaired) are provided in the "Note to Form FDA 3542a for U.S. Patent 6,399,632 submitted herewith for NDA 21909 (Allegra ODT); Note to Question 4.2(a). |

**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 |
|---|---|
| Charlotte L. Barney | 9/11/06 |

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

**Check applicable box and provide information below.**

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

| | |
|---|---|
| Name<br>Charlotte L. Barney<br>Associate General Counsel, US Patent Litigation | |
| Address<br>Sanofi Aventis Pharmaceuticals Inc.<br>1041 Route 202-206<br>P.O. Box 6800 | City/State<br>Bridgewater, New Jersey |
| ZIP Code<br>08807-0800 | Telephone Number<br>908-231-4551 |
| FAX Number *(if available)*<br>908-231-2840 | E-Mail Address *(if available)*<br>charlote.barney@sanofi-aventis.com |

Notes to Form FDA 3542a for U.S. Patent No. 6,399,632 submitted herewith for NDA 21909 (Allegra ODT)

Note to Question 4.2(a): The proposed 1) **INDICATIONS AND USAGE,** 2) a relevant section from proposed **PRECAUTIONS** (Drug Interactions), and 3) a relevant section from proposed **CLINICAL PHARMACOLOGY** (Special Populations—Hepatically Impaired) are as follows:

## INDICATIONS AND USAGE

**Seasonal Allergic Rhinitis**
ALLEGRA is indicated for the relief of symptoms associated with seasonal allergic rhinitis in adults and children 2 years of age and older. Symptoms treated effectively were sneezing, rhinorrhea, itchy nose/palate/throat, itchy/watery/red eyes.

**Chronic Idiopathic Urticaria**
ALLEGRA is indicated for treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 6 months of age and older. It significantly reduces pruritus and the number of wheals.

## PRECAUTIONS

**Drug Interactions**

Fexofenadine has been shown to exhibit minimal (ca. 5%) metabolism. However, co-administration of fexofenadine hydrochloride with either ketoconazole or erythromycin led to increased plasma concentrations of fexofenadine hydrochloride in healthy adult subjects. Fexofenadine had no effect on the pharmacokinetics of either erythromycin and ketoconazole. In 2 separate studies in healthy adult subjects, fexofenadine hydrochloride 120 mg twice daily (240 mg total daily dose) was co-administered with either erythromycin 500 mg every 8 hours or ketoconazole 400 mg once daily under steady state conditions to healthy adult subjects (n=24, each study). No differences in adverse events or QTc interval were observed when subjects were administered fexofenadine hydrochloride alone or in combination with either erythromycin or ketoconazole. The findings of these studies are summarized in the following table:

**Effects on steady-state fexofenadine pharmacokinetics after 7 days of co-administration with fexofenadine hydrochloride 120mg every 12 hours in healthy adult subjects (n=24)**

| *Concomitant Drug* | $C_{maxSS}$ *(Peak plasma concentration)* | $AUC_{ss(0\text{-}12h)}$ *(Extent of systemic exposure)* |
|---|---|---|
| Erythromycin (500mg every 8 hours) | +82% | +109% |
| Ketoconazole (400mg once daily) | +135% | +164% |

The changes in plasma levels were within the range of plasma levels achieved in adequate and well-controlled clinical trials.

The mechanism of these interactions has been evaluated in *in vitro*, *in situ* and *in vivo* animal models. These studies indicate that ketoconazole or erythromycin co-administration enhances fexofenadine gastrointestinal absorption. The observed increase in the bioavailability of fexofenadine may be due to transport-related effects, such a p-glycoprotein. In vivo animal studies also suggest that in addition to enhancing absorption, ketoconazole decreases fexofenadine gastrointestinal secretion, while erythromycin may also decrease biliary excretion.

## CLINICAL PHARMACOLOGY

**Special Populations**
Pharmacokinetics in renally and hepatically impaired subjects and geriatric subjects, obtained after a single does of 80 mg fexofenadine hydrochloride, were compared to those from healthy subjects in a separate study of similar design.

**Hepatic Impairment.** The pharmacokinetics of fexofenadine hydrochloride in subjects with hepatic disease did not differ substantially from that observed in healthy subjects.

# EXCLUSIVITY SUMMARY

NDA # 21-909 SUPPL # HFD # 570

Trade Name Allegra ODT

Generic Name fexofenadine

Applicant Name sanofi-aventis

Approval Date, If Known

## PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

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

YES ☒ NO ☐

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

505(b)(1)

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

YES ☐ NO ☒

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

This application relies on a comparison of the bioavailability and bioequivalence of the proposed new drug to that of an approved reference product, Allegra (fexofenadine HCl) Tablets, 30 mg. No clinical efficacy studies were required to support this application.

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# 20-625 | Allegra oral capsule 60mg |
| NDA# 20-786 | Allegra D 24 hour tablet |
| NDA# 20-872 | Allegra Tablet, oral |

2. Combination product.

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

YES ☐ NO ☐

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

NDA#

NDA#

NDA#

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

## PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

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

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

summary for that investigation.

YES ☐ NO ☒

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

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

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

YES ☐ NO ☐

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

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

YES ☐ NO ☐

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

YES ☐ NO ☐

If yes, explain:

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

YES ☐ NO ☐

If yes, explain:

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

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

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

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

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

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

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

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

If you have answered "yes" for one or more investigation, identify the NDA in which a

similar investigation was relied on:

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

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

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

Investigation #1

IND # YES ☐ ! NO ☐
! Explain:

Investigation #2

IND # YES ☐ ! NO ☐
! Explain:

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

Investigation #1

YES ☐ ! NO ☐

Explain: ! Explain:

Investigation #2 !
!
YES ☐ ! NO ☐
Explain: ! 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: Lori A. Garcia, R.Ph.
Title: Regulatory Project Manager
Date: July 19, 2007

Name of Office/Division Director signing form: Badrul A. Chowdhury, M.D., Ph.D.
Title: Division Director

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

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

/s/

**Badrul Chowdhury**
**7/26/2007 04:38:36 PM**

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# PEDIATRIC PAGE

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

NDA/BLA # : 21-909 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: September 29, 2006 PDUFA Goal Date: July 29, 2007

HFD 570 Trade and generic names/dosage form: Allegra (fexofenadine HCl) Orally Disintegrating Tablets, 30mg

Applicant: Sanofi Aventis Therapeutic Class: 3S

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

- ☐ [redacted]. 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):** 2

Indication #1: Twice daily (BID) treatment of seasonal allergic rhinitis (SAR) in children 6 to 11 years of age.

**Is this an orphan indication?**

- ☐ Yes. PREA does not apply. Skip to signature block.
- ☐ [redacted]. Please proceed to the next question.

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

- ☐ Yes: Please proceed to Section A.
- ☐ [redacted] No: Please check all that apply: [redacted] Partial Waiver [redacted] 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 'ttachment 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.__< 2 years___ 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—no meaningful benefit over existing therapies**
- ☐ **[redacted]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.__2___ Tanner Stage_____**
**Max_____ kg_____ mo._____ yr.__<6__ 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**
- ☐ **[redacted] Adult studies ready for approval**
- ☐ **[redacted]Formulation needed—[redacted]**

**Other:_____**

**Date studies are due (mm/dd/yy): __7/31/2010_____**

*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_____**

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

**This page was completed by:**

*{See appended electronic signature page}*

**Lori Garcia, RPh, Regulatory Project Manager**

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

**(Revised: 10/10/2006)**

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

Indication #2: _____Treatment of uncomplicated manifestations of CIU in children 6 to 11 years of age.

**Is this an orphan indication?**

- ☐ **Yes. PREA does not apply. Skip to signature block.**
- ☐ [redacted] **Please proceed to the next question.**

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

- ☐ **Yes: Please proceed to Section A.**
- ☐ [redacted] **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.__< 2 years___ Tanner Stage_____**
**Max_____ kg_____ mo._____ yr._____ Tanner Stage_____**

**Reason(s) for partial waiver:**

- ☐ [redacted]**Products in this class for this indication have been studied/labeled for pediatric population** [redacted]**—no meaningful benefit over existing therapies**
- ☐ **Disease/condition does not exist in children**
- ☐ [redacted]**Too few children with disease to study**—[redacted]
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**
- ☐ **Other:_____**

*f 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.** 2 **Tanner Stage**_____
**Max**_____ **kg**_____ **mo.**_____ **yr.** < 6 **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**
- [redacted] **Formulation needed**
- ☐ **Other:**_____

**Date studies are due (mm/dd/yy):** 07/31/2010

*f 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}*

_____
**Lori Garcia, RPh, 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 is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

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/s/

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Lori Garcia
7/26/2007 01:40:32 PM

sanofi aventis

Because health matters

**Debarment Certification**

September 28, 2006

Sanofi-aventis US LLC, hereby certifies that it has not used and will not use in any capacity the services of any person debarred pursuant to section 306(a) and (b) of the Federal Food, Drug and Cosmetic Act [21 U.S.C. 335(a) and (b)] in connection with this application.

Mark W. Moyer

Mark Moyer
V.P., Deputy Head, US Regulatory Development
Tel (609) 889 6417 or Lori Birkenberger, Ph.D. (908) 231 3126

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**Food and Drug Administration**
**Center for Drug Evaluation and Research**
**Office of Drug Evaluation II**

## Memorandum of Facsimile Correspondence

Date: July 18, 2007

To: Mary Beth Wigley
Sanofi-aventis

Fax: 610-889-6993

Phone: 610-889-6792

From: Lori Garcia, R.Ph.
Regulatory Project Manager
Division of Pulmonary and Allergy Products

Subject: FDA-revised labeling/NDA 21-909



Thank you.

NDA 21-909
Sanofi-aventis

Attention: Mary Beth Wigley, B.S., M.S.
Assistant Director, Regulatory Development
Corporate Regulatory Affairs

Dear Ms. Wigley:

Please refer to your new drug application dated September 28, 2006, received September 29, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Allegra (fexofenadine hydrochloride) Orally Disintegrating Tablets, 30mg.

We have reviewed the draft labeling submitted June 29, 2007, and our proposed revisions are provided in the attached labeling. Explanatory comments corresponding to the numbered revisions in the attached label are provided at the end of the document. We request that you submit your revised draft labeling and/or comments by July 20, 2007.

If you have any questions, call Lori Garcia, Regulatory Project Manager, at 301-796-1212.

# 22 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

✓ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

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/s/
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Lori Garcia
7/18/2007 04:08:29 PM
CSO

# MEMORANDUM

**To:** **Lori Garcia, RPh**
**Division of Pulmonary and Allergy Products**

**From:** **Iris Masucci, PharmD, BCPS**
**Division of Drug Marketing, Advertising, and Communications for the Study Endpoints and Label Development (SEALD) Team, OND**

**Date:** **July 12, 2007**

**Re:** **Comments on draft labeling for Allegra (fexofenadine)**
**NDA 21-909**

---

We have reviewed the proposed label for Allegra (sponsor version dated 6/29/07) and offer the following comments. These comments are based on Title 21 of the Code of Federal Regulations (201.56 and 201.57), the preamble to the Final Rule, labeling Guidances, and FDA recommendations to provide for labeling quality and consistency across review divisions. We recognize that final labeling decisions rest with the review division after a full review of the submitted data.

## GENERAL COMMENTS

- All tables in the Full Prescribing Information (FPI) should be numbered. Please revise.

## HIGHLIGHTS

- *"ALLEGRA® (fexofenadine hydrochloride) tablets, ODT (orally disintegrating tablets) and oral suspension"*

[redacted] b(4)

**Recent Major Changes**

[redacted] b(4)

**Indications and Usage**

- [redacted] b(4)

According to Bill Pierce of the SEALD team, the proper pharmacologic classification for fexofenadine is "histamine$_1$ ($H_1$)-receptor antagonist." The word [redacted] should be deleted here [redacted] b(4)

- [redacted] b(4)

  Should this statement include the qualifier "... of uncomplicated skin manifestations of ..." from the FPI? Would the omission of this language in any way broaden the indication? If so, we recommend that it be included in the Highlights indication.

**Dosage and Administration**

- We suggest adding an extra return between the section heading and the table.
- For ease of reading, we recommend that some of the footnoted information from the table be changed to bullets, leaving only a few as footnotes. Note that we have changed the column headers to bolded type and added the cross-references in parentheses. We suggest:

b(4)

- ALLEGRA tablets: Take with water (2.1)
- ALLEGRA ODT: Take on an empty stomach; allow to disintegrate on the tongue and swallow with or without water; do not remove from original blister package until time of administration; do not break or use partial tablets (2.2)

[redacted] b(4)

**Contraindications**

- [redacted] b(4)

  We recommend this statement be reworded slightly to [redacted] This language is more precise and is consistent with the wording in the Xyzal label.

**Adverse Reactions**

- We recommend slight revisions to avoid use of the phrase "were more frequently reported" because we don't say "more frequently than what." We suggest:

b(4)

b(4)

- *"The most common adverse reactions (≥ 2%) in subjects age 12 years and older were headache, back pain, [redacted] dizziness, stomach discomfort, and pain in extremity."*

We recommend deleting [redacted] b(4)
Not all adverse reactions from the FPI need to be listed in Highlights.

**Drug Interactions**

- If the interaction with antacids is the only interaction to be included in Highlights, it should be 7.1 [redacted] b(4)

- Please consider adding the interaction with fruit juice to this section in Highlights. Alternatively, this information could be incorporated into the Dosage and Administration section where we say to take with water (e.g., "Take with water, not fruit juice" or something similar).

**Use in Specific Populations**

- Because the information presented in this section on use in pregnancy and in nursing mothers is very standard, it may be deleted entirely from Highlights. If specific risks or clinical recommendations other than these "generic" ones existed, then they should certainly be in Highlights. The inclusion of these is a decision for the review team.

**Revision Date**

- Please ensure that the month/year of approval is filled in when the label is finalized. Additionally, the brackets around the date should be deleted and the preferred formatting for this line is to have the text aligned with the right side of the column (right-justified).

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**CONTENTS**

- Under "2 Dosage and Administration," all words should begin with capital letters to be consistent with the rest of the Contents section. Please make the corresponding changes in the FPI headers as well.

- Once the FPI has been finalized, the Contents must be updated to ensure accuracy of the numbering and section titles. Then, any corresponding changes should be made to the Highlights and cross-references throughout the label.

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## FULL PRESCRIBING INFORMATION

b(4)

### ALLEGRA tablets

- The recommendation to take the tablets with water seems inadequate to convey that they shouldn't be taken with fruit juice. We recommend additional language clarifying this recommendation, with a cross-reference to the full discussion of the interaction in section 7.3.

### 2.2 ALLEGRA ODT

- *"ALLEGRA ODT is intended for use only in children 6 to 11 years of age."*

  The phrase "is intended for" seems somewhat vague and unusual for labeling. Can we say something stronger, e.g., "is approved for use only in.." or something similar?

### 4 CONTRAINDICATIONS

- [redacted] b(4)

  As in Highlights, we recommend specifically mentioning fexofenadine in this sentence.

### 6.1 Clinical Studies Experience

- In the titles of each of the tables in this section, we recommend adding that the reactions listed were those both >X% and more common than with placebo.

### 7 Drug Interactions

- As mentioned under Highlights, we suggest that the interactions in this section be reordered so the most important ones clinically appear first.

- This section of the FPI should present the broad clinical recommendations of interactions (e.g., adjust doses, stagger administration times, etc.). Any detailed data from pharmacokinetic drug interaction studies should be presented in "12.3 Pharmacokinetics" under a subheading for drug interaction studies. The broad recommendations given here should cross-reference to 12.3 as appropriate.

### Erythromycin and Ketoconazole

b(4)

- *"Fexofenadine has been shown to exhibit minimal (ca. 5%) metabolism."*

  What is meant by "ca. 5%"? This reviewer is not familiar with this. Please consider if it needs to be rewritten or deleted for clarity.

- As noted above, we recommend that the detailed data from the interaction studies be presented under 12.3.

- *"The changes in plasma levels were within the range of plasma levels achieved in adequate and well-controlled clinical trials."*

  Regardless of the final placement of this sentence in the label, we suggest deleting "adequate and well-controlled." This is more of a regulatory term and does not usually appear in labeling. Simply saying, "... achieved in the clinical trials" would be adequate.

**Antacids**

- *"Fexofenadine hydrochloride should not be taken closely in time with aluminum and magnesium containing antacids."* b(4)

  We suggest moving this sentence to the beginning of this section. This change will present the clinical recommendation first, followed by the data that support it.

  Can we give any better recommendation on spacing the administration of the two drugs than "not closely in time" together? This seems somewhat vague. Most labels recommending staggered administration times are more specific (e.g., do not take 2 hours before or 2 hours after taking antacids.) Are such data available here?

- We suggest deleting the brand name '——— from this section. In general, brand names are not used in labels to describe other products. b(4)

**7.3 Fruit Juices**

- *"ALLEGRA ODT can be taken with or without water [see Clinical Pharmacology (12.3) and Dosage and Administration (2.2)]."*

  This sentence should be deleted because it does not discuss interactions with fruit juices and because it is adequately addressed under Dosage and Administration.

**8.4 Pediatric Use**

- Where possible, we suggest adding cross-references in paragraphs 2 and 3 in this section to the pediatric clinical studies or pharmacokinetic studies that are presented elsewhere in the label.

- *"The safety and effectiveness of fexofenadine hydrochloride in pediatric patients under 6 months of age have not been established."*

  We suggest that this sentence be moved to the end of the first paragraph in this section. This change will avoid its being overlooked and will keep all similar information together.

**10 Overdosage**

- The second paragraph in this section should be indented.

**12.2 Pharmacodynamics**

- [redacted] b(4)

**14.1 Seasonal Allergic Rhinitis**

- *"In 1 clinical trial conducted with ALLEGRA 60 mg capsules, and in 1 clinical trial conducted with ALLEGRA-D 12 Hour extended release tablets, onset of action was seen within 1 to 3 hours."*

  [redacted] b(4)

- *"Administration of a 30 mg dose to pediatric subjects 2 to 11 years of age produced exposures comparable to those seen with a dose of 60 mg administered to adults. [See Clinical Pharmacology (12.3)]."*

  [redacted] b(4)

**17 Patient Counseling Information**

- [redacted] b(4)

- *"For ALLEGRA tablets: Advise patients to take the ALLEGRA tablets with water."*

  As above, please consider adding the recommendation not to take with fruit juice to this section.

- *"Phenylketonurics: ALLEGRA ODT contains phenylalanine, a component of aspartame. Each 30-mg ALLEGRA ODT contains 5.3 mg phenylalanine. ALLEGRA products other than ALLEGRA ODT do not contain phenylalanine."*

  [redacted] b(4)

  Most labels for drugs containing phenylalanine discuss phenylketonurics information as a Precaution (in the old labeling format) and repeat it under Patient Information.

  Please delete the dash in "30-mg."

- Please delete "Rx only" at the end of the label. This statement is required on cartons, but not in package inserts.

- Please delete the copyright date at the end of the label. The revision date at the end of Highlights is intended to replace this date which has traditionally appeared at the end of labels.

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/s/
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Iris Masucci
7/12/2007 01:53:28 PM
DDMAC REVIEWER

Laurie Burke
7/16/2007 07:22:00 PM
INTERDISCIPLINARY

**Food and Drug Administration**
**Center for Drug Evaluation and Research**
**Office of Drug Evaluation II**

## Memorandum of Facsimile Correspondence

Date: June 14, 2007

To: Mary Beth Wigley
Sanofi-aventis

Fax: 610-889-6993

Phone: 610-889-6792

From: Lori Garcia, R.Ph.
Regulatory Project Manager
Division of Pulmonary and Allergy Products

Subject: FDA-revised labeling/NDA 21-909



Thank you.

NDA 21-909
Sanofi-aventis

Attention: Mary Beth Wigley, B.S., M.S.
Assistant Director, Regulatory Development
Corporate Regulatory Affairs

Dear Ms. Wigley:

Please refer to your new drug application dated September 28, 2006, received September 29, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Allegra (fexofenadine hydrochloride) Orally Disintegrating Tablets, 30mg.

We have reviewed the draft labeling submitted November 10, 2006, and our proposed revisions are provided in the attached labeling. FDA-proposed insertions are underlined and deletions are in strike-out. Be advised that these labeling changes are not necessarily the Agency's final recommendations and that additional labeling changes may be forthcoming as the label is reviewed by other offices within the Agency.

We request that you submit your revised draft labeling and/or comments by June 21, 2007.

If you have any questions, call Lori Garcia, Regulatory Project Manager, at 301-796-1212.

# 23 Page(s) Withheld

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✓ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

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/s/

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Lori Garcia
6/14/2007 03:20:18 PM
CSO

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**MEMORANDUM**

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

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DATE: May 10, 2007

TO: Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary and Allergy Products.

FROM: Jagan Mohan R. Parepally, Ph.D.
Division of Scientific Investigations (HFD-48)

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

SUBJECT: Review of EIRs Covering NDA 21-909, Allegra (fexofenadine HCl) Orally Disintegrating Tablets (ODT) 30 mg, Sponsored by Sanofi Aventis Pharmaceuticals Inc., Bridgewater, NJ

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

**Study MO16455H/1007**: Two-way Crossover, Randomized, Open-label Pivotal Bioequivalence Study Comparing the Fexofenadine Hydrochloride Orally Disintegrating Tablet (ODT) Formulation (30 mg) to the Marketed Allegra Tablet (30 mg) in Healthy Adult Subjects.

**Study MO16455H/1008**: Two-way Crossover, Randomized, Open-label Study Comparing the Bioequivalence of the Fexofenadine Hydrochloride Orally Disintegrating Tablet (ODT) Formulation (30 mg) Given with and without Water to Healthy Adult Subjects.

The clinical portions of Studies MO16455H/1007 and MO16455H/10078 were conducted at Bio-Kinetic Clinical Applications, Springfield, MO. Analytical portions of both

studies were conducted at [redacted] (formerly [redacted] No FDA Form 483 was issued at the conclusion of the inspections at [redacted] (2/26-3/2/07) and Bio-Kinetic Clinical Applications (03/29/07-04/05/07). DSI's evaluation of the inspectional findings follows: b(4)

**Clinical Site: Bio-Kinetic Clinical Applications, Springfield, MO**
No significant observations.

**Analytical Site:** [redacted] **(formerly** [redacted] b(4)
No significant observations.

**Conclusion:**

Following our evaluation of the inspectional findings, DSI concludes that the inspections did not reveal any significant deficiencies.

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

Jagan Mohan R. Parepally, Ph.D.

**Final Classification:**

**Bio-Kinetic Clinical Applications - NAI (Clinical)** b(4)
[redacted] **- NAI (Analytical)**

cc:
HFD-45/RF
HFD-48/Parepally/Himaya/CF
DPAP/Garcia
DCP2/Fadiran/Al Habet
HFR-SE300/Cronenwett
HFR-CE700/Kuchenthal
Draft: JP 05/10/07
Edit: MFS 05/11/07
DSI 5741; O:\BE\eircover\21909san.fex.doc
FACTS

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/s/

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Jagan Parepally
5/15/2007 01:52:00 PM
PHARMACOLOGIST
Dr. Viswanathan signed the paper copy on May 15, 2007

**Food and Drug Administration**
**Center for Drug Evaluation and Research**
**Office of Drug Evaluation II**

# FACSIMILE TRANSMITTAL SHEET

**DATE:** April 26, 2007

| | |
|---|---|
| **To:** Mary Beth Wigley | **From:** LCDR Lori Garcia<br>Regulatory Project Manager |
| **Company:** Sanofi-aventis | |
| **Fax number:** (610) 889-6993 | **Fax number:** 301-796-9718 |
| **Phone number:** (610) 889-6792 | **Phone number:** 301-796-1212 |

**Subject:** **NDA 21-909/CMC discipline review letter**

**Total no. of pages including cover:** 4

**Comments:**

**Document to be mailed:** xx_YES _NO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-909

**DISCIPLINE REVIEW LETTER**

Sanofi-Aventis
9 Great Valley Parkway
P.O. Box 3026
Malvern, PA 19355

Attention: Mary Beth Wigley

Dear Ms. Wigley:

Please refer to your September 28, 2006, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Allegra (fexofenadine hydrochloride) orally disintegrating tablets.

We also refer to your submissions dated January 18, and February 8, 2007.

Our review of the Chemistry, Manufacturing and Controls section of your submission is complete, and we have identified the following deficiencies:

1.

2.

b(4)

3.

4.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are

preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

If you have any questions, call Lori Garcia, Regulatory Project Manager, at 301-796-1212.

Sincerely,

*{See appended electronic signature page}*

Blair A. Fraser, Ph.D.
Chief, Branch II
Division of Pre-Marketing Assessment I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

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Blair Fraser
4/25/2007 09:01:23 PM

**Food and Drug Administration**
**Center for Drug Evaluation and Research**
**Office of Drug Evaluation II**

# Memorandum of Facsimile Correspondence

Date: April 5, 2007

To: Mary Beth Wigley
Sanofi-aventis

Fax: 610-889-6993

Phone: 610-889-6792

From: Lori Garcia, R.Ph.
Regulatory Project Manager
Division of Pulmonary and Allergy Products

Subject: FDA response to 1/11/07 submission for NDA 21-909



Thank you.

NDA 21-909
Sanofi-aventis

Dear Ms. Wigley:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Allegra (fexofenadine hydrochloride) Orally Disintegrating Tablet, 30mg.

We also refer to your submission dated January 11, 2007, requesting FDA clarification of several labeling comments provided in the Filing Communication letter dated December 12, 2006.

We have completed the review of your submission, and have the following responses.

**FDA Comment 7:**
The Word version (.doc) of the labeling submitted on September 28, 2006, does not match the SPL version (.xml) submitted on November 10, 2006. The formatting and text of these 2 versions should be the same.

Sanofi-aventis response:
Please clarify which parts of the formatting and text are not the same between the SPL and the Word versions. Some of these differences are due to the stylesheet provided by the agency and used to view the SPL. Also, please inform us if the agency's expectation is that the Word version and the SPL version are 100% identical.

FDA clarification:

At the moment, the expectation is that the content of the Word version (the final agreed-upon version) will match the final SPLversion, to the extent possible. The two versions do not have to match during the review cycle because we are not expecting you to submit multiple copies of SPL during labeling discussions. We acknowledge that there will be certain aspects of the formatting that will be different in SPL since it uses the current SPL stylesheet and it addends further information (e.g. Patient information section; med guides, etc), so in these instances it is not expected that the Word document and SPL version be identical. However, you should accurately represent the formatting of the content of SPL (e.g. sections, subsections italics, bolding, etc.) in the Word document. sections, subsections italics, bolding, etc.) in the same way as in approved labeling.

**FDA Comment 9**:
The drug names must be followed by the drug's dosage form(s) and route of administration. Please correct and include all dosage forms that are provided for by this labeling. [See 21 CFR 201.57(a)(2)].

Sanofi-aventis response:
The information included in this section is governed by the stylesheet used to view the SPL (.xml) file. This issue was discussed at an FDA Webinar in December. The department at the agency that is responsible for the stylesheet is aware of this issue but have not reached a solution as yet. Until a solution is found, we are currently unable to correct this issue from our end.

FDA clarification:
We will address this issue during labeling discussions.

**FDA Comment 10:**
The phrase [redacted] after "Allegra (fexofenadine hydrochloride) Tablet, Orally Disintegrating" can be omitted. It is only necessary to include the route of administration if it is not typical for the dosage form. b(4)

Sanofi-aventis response:
The information included in this section is governed by the stylesheet used to view the SPL (.xml) file. See sanofi-aventis response to Comment 9.

FDA clarification:
We will address this issue during labeling discussions.

**FDA Comment 12:**
Under RECENT MAJOR CHANGES, the heading, and if appropriate, the subheading of the labeling section affected by the change must be listed together. Do not include the type of change [See 21 CFR 201.57(a)(5)]. In addition, the corresponding new of modified text under the sections in the Full Prescribing Information (FPI) must be marked with a vertical line ("margin mark") on the left edge. [See 21 CFR 201.57 (d)(9) and Implementation Guidance]

Sanofi-aventis response:
The agency has requested that the new or modified text in the sections identified under RECENT MAJOR CHANGES should be marked in the Full Prescribing Information (FPI) with a vertical line on the left edge. Our understanding is that the printed version of the USPI needed to identify the modified text as described above, and not the draft submitted labeling. Please clarify if this type of identification of changes is required in submitted draft labeling.
Also, this type of format change cannot be formatted in the SPL version of the USPI.

FDA clarification:
Draft labeling should identify all changes that are proposed for the printed version of the USPI. We can not assume that you are aware of this formatting requirement and that it will be applied correctly in the printed version. New or modified text in the sections identified under RECENT MAJOR CHANGES should be marked in the Full Prescribing Information (FPI) with a vertical line on the left edge in the both the Word and SPL versions of the labeling. Please note that the vertical line is displayed next to recent

major change text by the stylesheet when the recent major text is tagged using <content styleCode="xmChange">. This is described in the SPL Implementation Guide.

**FDA Comment 15:**
Under DOSAGE AND ADMINISTRATION, do not use the asterisk (*) to footnote information in the tables in Highlights since this symbol is used in the Table of Contents (i.e. *Sections or subsections omitted from the full prescribing information are not listed). Use a different symbol.

Sanofi-aventis response:
There is a hierarchy of footnotes that is used within the stylesheet for the SPL version with includes the asterisk (*) as the first one to be used. As we are not able to modify the stylesheet, we are not able to modify this footnote in the DOSAGE AND ADMINISTRATION table in the Highlights section as requested in comment 15. We would consider any agency suggestion to help resolve this issue. Currently, the Word version uses a different set of symbols for the footnotes in the table in Highlights.

FDA clarification:
Please contact spl@fda.hhs.org for technical advice.

**FDA Comment 17:**
If the WARNINGS AND PRECAUTIONS section is present in Highlights, then it must also be included in the Contents and in the Full Prescribing Information (FPI).

Sanofi-aventis response:
Based on the regulations for the Highlights section 21 CFR 201.56 (d)(1) identifies that the WARNINGS AND PRECAUTIONS section must be included in the Highlights section. However, our understanding based on CFR 201.56 (d)(4) is that if there is no relevant information in a section, that it may be omitted in the Full Prescribing Information, with the exception of the CONTRAINDICATIONS section. Is it the agency's view that the WARNINGS AND PRECAUTIONS section be included in the Highlights, Table of Contents and the Full Prescribing Information even though there is no text in this section?

FDA clarification:
No, that is not the Agency's view. This comment would apply if clinically significant information as required under 21 CFR 201.57(c)(6) was included in the WARNINGS AND PRECAUTIONS section of Highlights. We acknowledge that the intent of this comment was not clear. Our intent was to state that the WARNINGS AND PRECAUTIONS section should be omitted from Highlights under 21 CFR 201.56(d)(4) since it is clearly not applicable.

**FDA Comment 18:**
Do not include pregnancy category in Highlights [See comment #34 Preamble].

Sanofi-aventis response:
The Agency has requested to remove the pregnancy category. Does this request pertain to only the "Category C" designation or to the pregnancy statement as a whole?

FDA clarification:
We recommend deletion of the Pregnant Women statement as a whole. The Category C designation ***must not*** be included in Highlights. If you choose to refer to "Pregnant Women" in the Use in Specific Populations section, a concise summary of any clinically important differences in response or recommendations for use in this specific population should be included.

b(4)

Furthermore, reference to Nursing Mothers in the Highlights section should also be considered for deletion. Be advised that if all references to specific populations are deleted from this section, the section itself should be deleted from Highlights.

**FDA Comment 21:**
You refer to adverse reactions as [redacted] Please refer to the "Guidance for Industry: Adverse Reactions Sections of Labeling for Human Prescription Drug and Biological Products – Content and Format" available at http://www.fda.gov/cder/guidance and revise your adverse reactions section accordingly. b(4)

Sanofi-aventis response:
During previous forums and conferences with the agency regarding the Adverse Reactions section, it has been implied that sponsors of older drug products would not be required to search old databases to re-write this section. However, the adverse reaction section would need to be reviewed to ensure that events clearly not associated with the drug product be removed from the section. In this comment, is it the agency's intention to request that the Adverse Reactions section for this drug product be rewritten to include only adverse reactions that are thought to be reasonably associated with the drug product as opposed to the currently approved labeling for this section?

FDA clarification:
Generally, we recommend that you review your current labeling and delete those events where there is no basis to believe that a causal relationship could possibly exist between the occurrence of the event and use of the drug. The final decision about whether or not a full re-analysis of the data is necessary and about final terminology and presentation of data in the Adverse Reactions section is determined by the Review Division.

**FDA Comment 22:**
Indent all paragraphs, headings, subheading throughout the FPI. For overall FPI formatting, refer to http://www.fda.gov/cder/regulatory/physLabel/default.htm for fictitious examples of labeling in the new format.

Sanofi-aventis response:
We agree to comply with the agency's request in the Word (.doc) version, however if we also comply with this request in the SPL (.xml) version, we would be inconsistent with the Implementation guide of the SPL.

FDA clarification:
With the implementation of the new format and content, we have clarified this position. The subheadings are required to be indented in the "Contents" (201.57(d)(10)), but not in the FPI. The "Imdicon" example indents subheadings, whereas the "Fantom" example does not. There is no preferred approach, so you should use your judgment.

**FDA Comment 26:**
Under HOW SUPPLIED/STORAGE AND HANDLING, you refer to [See USP Controlled Room Temperature]. Please provide a temperature range for controlled temperature. [See 21 CFR 201.57(c)(17)]

Sanofi-aventis response:
Could you please provide clarification for this comment, as the temperature range for controlled room temperature has been provided in the HOW SUPPLIED section for the specific dosage forms. A minor modification to include the approved labeling text with the USP statement within the same sentence can been made. An example has been provided for the Allegra Tablets information;
"Store ALLEGRA Tablets at controlled room temperature 20-25°C (68-77°F) (See USP Controlled Room Temperature)."

FDA clarification:
This issue can be further addressed during labeling discussions.

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/s/
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Lori Garcia
4/5/2007 11:44:37 AM
CSO

**FOOD AND DRUG ADMINISTRATION**
**Center for Drug Evaluation and Research**
**Division of Drug Marketing, Advertising, and Communications**

# Memorandum

**Date:** March 8, 2007

**To:** Lori Garcia, RPh, Regulatory Project Manager
Division of Pulmonary and Allergy Products

**From:** Michelle Safarik, PA-C, Regulatory Review Officer
Division of Drug Marketing, Advertising, and Communications

**Subject:** NDA 21-909
DDMAC labeling comments for Allegra (fexofenadine hydrochloride) ODT (orally disintegrating tablets)

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Per your consult request dated November 28, 2006, DDMAC has reviewed the proposed product labeling (PI) and proposed carton and container labeling for Allegra ODT, and we offer the following comments. While we acknowledge this NDA provides for a new formulation to the fexofenadine product line, DDMAC has reviewed the entire label and are thus commenting on other sections of the label that are already approved.

## PI

### Highlights

Indications and Usage

b(4

1. [redacted]

   Is it appropriate to include [redacted] when discussing Indications and Usage? If not, we recommend deletion.

b(4)

2. Is it appropriate to include the limitation to the seasonal allergic rhinitis (SAR) indication that use is intended for patients ≥2 years of age, and to include the limitation to the chronic idiopathic urticaria (CIU) indication that use is intended for patients ≥6 months of age?

Adverse Reactions

1. Is it appropriate to include only headache and vomiting as the most common adverse reactions for a drug that has two indications and intended uses for various patient populations?

## 2.2 ALLEGRA ODT

1. "ALLEGRA ODT is designed to [redacted] disintegrate on the tongue..." b(4)

   Would it be possible to provide context for [redacted]? b(4)

## 6.1 Seasonal Allergic Rhinitis

1. We recommend American English spellings for "diarrhoea" and "rhinorrhoea" (Table 3).

## 11 Description

1. [redacted]

   Would it be possible to provide context for [redacted]? b(4)

## 12.3 Pharmacokinetics

1. [redacted] b(4)

   [redacted] is promotional in tone; we recommend deletion since context is provided later in the paragraphs (i.e., 2.6 hours post-dose, 2.0 hours following oral administration). b(4)

## Carton and Container Labeling

We have reviewed the proposed carton and container labeling and have no comments at this time.

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/s/
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Michelle Safarik
3/8/2007 04:49:21 PM
DDMAC REVIEWER

Appears This Way
On Original

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

# FACSIMILE TRANSMITTAL SHEET

**DATE: February 16, 2007**

| | |
|---|---|
| **To:** Lori Birkenberger | **From:** LCDR Lori Garcia<br>Regulatory Project Manager |
| **Company:** sanofi-aventis | Division of Pulmonary and Allergy Products |
| **Fax number:** (908) 541-5274 | **Fax number:** 301-796-9718 |
| **Phone number:** (908) 231-3126 | **Phone number:** 301-796-1212 |

**Subject:** NDA 21-909/1/23/07 tcon meeting minutes

**Total no. of pages including cover:** 5

**Comments:**

**Document to be mailed:** YES xNO

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

| | |
|---|---|
| **Meeting Type:** | Teleconference |
| **Meeting Category:** | Other |
| **Meeting Date and Time:** | January 23, 2007, 2:00pm-3:00pm EST |
| **Application Number:** | NDA 21-909 |
| **Product Name:** | Allegra ODT |
| **Received Briefing Package** | N/A |
| **Sponsor Name:** | sanofi-aventis |
| **Meeting Requestor:** | FDA |
| **Meeting Chair:** | Badrul A. Chowdhury, M.D., Ph.D. |
| **Meeting Recorder:** | Lori A. Garcia, R.Ph. |
| **Meeting Attendees:** | |

**FDA Attendees**
**Division of Pulmonary and Allergy Drug Products**
Badrul Chowdhury, M.D., Ph.D., Division Director
Charles Lee, M.D., Clinical Team Leader
Emmanuel Fadiran, Ph.D., ClinPharm Team Leader
Sayed Al Habet, Ph.D., ClinPharm Reviewer
Martin Haber, Ph.D., ONDQA Reviewer
Prasad Peri, Ph.D., ONDQA PAL
Lori Garcia, RPh., Regulatory Project Manager

**Sponsor Attendees**
**sanofi-aventis**

| | |
|---|---|
| Birkenberger, Lori | Regulatory Development |
| Plon, Judy | Axis Lead, Regulatory Development |
| Moyer, Mark | Deputy US Head, Regulatory Development |
| Shah, Mridul | Regulatory, CMC |
| Faustino, Marilia | Regulatory, CMC |
| Vudathala, Gopi | Regulatory, CMC |
| Kittner, Barbara | Clinical |
| Punwani, Naresh | Biopharmaceutics |
| Chrzan, Kazimierz | Analytical Science |
| Parrish, Marie | CMC Documentation |
| Dennie, Denise | Project Direction |

**CIMA Partners**

| | |
|---|---|
| Simonson, Philip G. | Regulatory |
| Khankari, Raj | Drug Delivery Technology |

## 1.0 BACKGROUND

FDA requested a meeting with sanofi-aventis to discuss the nomenclature for the Allegra ODT new drug application, NDA 21-909. FDA has identified two outstanding issues related to the nomenclature of the ODT drug product during the ongoing review of the NDA: tablet disintegration times of ≥ 30 seconds and a tablet size of ≥500 mg. The criteria for an ODT formulation were conveyed to sanofi-aventis during the March 8, 2005, pre-NDA meeting (see Meeting Minutes dated March 17, 2005), and are as follows.

*Criteria for ODT:*

- *disintegrate rapidly in the oral cavity.*
- *eliminate the need for use of water or chewing.*
- *recommended tablet weight to be less than 500 mg for compliance reasons, especially for children (if too big, dosage form may be partially spit out).*
- *in vitro disintegration with USP <701> to be less than 30 seconds.*

Sanofi-aventis was notified at this time that the application of the ODT dosage form nomenclature to their drug product would be a review issue.

The purpose of today's meeting is to convey the FDA's position on the nomenclature issue to sanofi-aventis, and to discuss and explore possible paths forward.

## 2.0 DISCUSSION

FDA noted that the intent of this teleconference was to inform sanofi-aventis of FDA's expectation regarding the nomenclature issue. FDA stated that for a product to be considered an "Orally Disintegrating Tablet (ODT)," it must dissolve in less than 30 seconds, and should not be greater than 500mg in size, per the internal policy of the Office of New Drug Quality Assurance (ONDQA). FDA suggested that sanofi-aventis may wish to consider reformulating their product, or using different nomenclature to identify their drug product. Sanofi-aventis inquired about the rationale behind ONDQA's policy. FDA noted that the policy was based on historical data and that there is a large database that meets the current criteria. FDA stated that a decision on approvability of the NDA has not been made yet. The NDA is still open and under review. FDA reiterated that the purpose of today's meeting was to inform sanofi-aventis of FDA's concerns regarding the ODT nomenclature, and to give sanofi-aventis the opportunity to address this issue during the current review cycle. FDA stated that it would review and consider any new names or other proposals to address the nomenclature issue that are submitted by sanofi-aventis. Sanofi-aventis indicated that the FDA approved, in the past year, an ODT that was more than 500 mg. In addition, sanofi-aventis offered to provide information on several marketed ODT drug products that weigh [redacted] b(4)
Sanofi-aventis also indicated that their disintegration method is different from the USP <701> method and that in their preliminary results with the USP method, disintegration times were around 29 seconds. The Agency indicated it would not comment on actions taken previously and that the evaluation of the disintegration method in the current NDA

is not yet complete. Sanofi-aventis asked if the nomenclature would still be an issue for FDA if 3 out of the 4 of the criteria were met. FDA replied that this would be a review issue.

## 3.0 ISSUES REQUIRING FURTHER DISCUSSION

FDA and/or sanofi-aventis may request a teleconference to revisit the nomenclature issue later in the review cycle, if needed.

## 4.0 ACTION ITEMS

No action items were identified during the meeting.

## 5.0 ATTACHMENTS AND HANDOUTS

No attachments of handouts were presented at the meeting.

Drafted: LGarcia/February 8, 2007

Initialed: PPeri/2.9.07
MHaber/2.12.07
EFadiran/2.9.07
CLee/2.16.07
BChowdhury/2.16.07

Finalized: LGarcia/February 16, 2007

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/s/
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Lori Garcia
2/16/2007 02:33:54 PM
CSO

| DEPARTMENT OF HEALTH AND HUMAN SERVICES<br>Food and Drug Administration | | | REQUEST FOR CONSULTATION | |
|---|---|---|---|---|
| TO *(Division/Office)*<br>OPS/PARS | | | FROM<br>ONDQA/DPA-1 | |
| DATE<br>1/24/2007 | IDA NO. | NDA NO.<br>21-909 | TYPE OF DOCUMENT<br>Electronic | DATE OF DOCUMENT<br>9/28/2006 |
| NAME OF DRUG<br>Allegra ODT | | PRIORITY CONSIDERATION<br>S | CLASSIFICATION OF DRUG | DESIRED COMPLETION DATE<br>3/28/2007 |
| NAME OF FIRM<br>Sanofi-aventis | | | | |

**REASON FOR REQUEST**

**I. GENERAL**

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ PMANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY kljsgkl
- ☐ PRE-NDA
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER *(Spectfy below)* Environmental Assessment

**II. BIOMETRICS**

| STATISTICAL EVALUATION | STATISTICAL APPLICATION BRANCH |
|---|---|
| ☐ TYPE A OR B NDA REVIEW | ☐ CHEMISTRY |
| ☐ END OF PHASE II MEETING | ☐ PHARMACOLOGY |
| ☐ CONTROLLED STUDIES | ☐ BIOPHARMACEUTICS |
| ☐ PROTOCOL REVIEW | ☐ OTHER _____ |
| ☐ OTHER _____ | |

**III. BIOPHARMACEUTICS**

- ☐ DISSOLUTION
- ☐ BIOAVAILABILITY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

**IV. DRUG EXPERIENCE**

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE E.G. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS *(List below in comments)*
- ☐ COMPARATIVE RISK ASSESSEMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

**V. SCIENTIFIC INVESTIGATIONS**

☐ CLINICAL ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS *(Attach additional sheets if necessary)*

Attention: Bai Nguyen, OPS
cc: Raanan Bloom, OPS
Please review EA

| SIGNATURE OF REQUESTER | METHOD OF DELIVERY *(Check One)*<br>☒ MAIL ☐ HAND |
|---|---|
| SIGNATURE OF RECEIVER | SIGNATURE OF DELIVERY |



PSC Media Arts (301) 443-1090 EF

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/s/

Martin Haber
1/24/2007 11:19:45 AM
CHEMIST

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

NDA # 21-909 Supplement # N/A Efficacy Supplement Type SE-

Proprietary Name: Allegra ODT
Established Name: fexofenadine hydrochloride orally disintegrating tablet
Strengths: 30mg

Applicant: sanofi aventis
Agent for Applicant (if applicable):

Date of Application: September 28, 2006
Date of Receipt: September 29, 2006
Date clock started after UN:
Date of Filing Meeting: November 17, 2006
Filing Date: November 28, 2006
Action Goal Date (optional): User Fee Goal Date: July 29, 2007

Indication(s) requested: SAR and CIU in children 6 to 11 years of age.

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.) 3
Other (orphan, OTC, etc.)

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 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: Exclusivity expires October 13, 2008

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 ☒

- Is the application affected by the Application Integrity Policy (AIP)? YES ☐ NO ☒
  If yes, explain:

- 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/2353fnl.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: IND 43,573; IND 62,912; IND 51,709

- 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) January 10, 2003 NO ☐
  If yes, distribute minutes before filing meeting.

- Pre-NDA Meeting(s)? Date(s) March 8, 2005 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? N/A ☒ YES ☐ NO ☐

## Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff?
  N/A 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: November 17, 2006

NDA #: N21-909

DRUG NAMES: Allegra ODT

APPLICANT: sanofi aventis

BACKGROUND: NDA provides for a 30mg orally disintegrating tablet formulation of Allegra. Indication: twice daily (BID) treatment of seasonal allergic rhinitis (SAR) and uncomplicated manifestations of CIU in children 6 to 11 years of age.

ATTENDEES: Charlie Lee, Joseph Sun, Prasad Peri, Badrul Chowdhury, Sayed Al-Habet, Tayo Fadiran, Lori Garcia

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

| **Discipline/Organization** | **Reviewer** |
|---|---|
| Medical: | Charlie Lee |
| Secondary Medical: | |
| Statistical: | Ted Guo |
| Pharmacology: | Larry Sancilio |
| Statistical Pharmacology: | |
| Chemistry: | Prasad Peri |
| Environmental Assessment (if needed): | |
| Biopharmaceutical: | Sayed Al Habet |
| Microbiology, sterility: | |
| Microbiology, clinical (for antimicrobial products only): | |
| DSI: | |
| OPS: | |
| Regulatory Project Management: | Lori Garcia |
| Other Consults: | |

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: No safety and efficacy studies conducted in this development program.
- 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? ☒ NO ☐
  YES

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):

**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.

Lori Garcia, R.Ph., Project Manager
Version 6/14/2006

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/s/

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Lori Garcia
1/3/2007 10:33:53 AM
CSO