CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201373Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

PATENT INFORMATION

Pursuant to initial NDA 21 CFR 314.53(d)(1) the patent information for this supplement is being submitted concurrently herewith by separate letter addressed to the Central Document Room.

Mary Beth Wigley

Mary Beth Wigley, B.S., M.S.

Assistant Director

Regulatory Research & Development Portfolio
Global Regulatory Affairs

Sanofi-aventis U.S. Inc.
on behalf of sanofi-aventis U.S. LLC

EXCLUSIVITY SUMMARY

NDA # 201373 SUPPL # HFD # 560

Trade Name Children's Allegra Allergy and Children's Allegra Hives

Generic Name Fexofenadine HCl

Applicant Name sanofi-aventis, LLC

Approval Date, If Known January 24, 2011

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

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

YES ☒ NO ☐

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

SE6

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

YES ☐ NO ☒

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

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

d) Did the applicant request exclusivity?

YES ☒ NO ☐

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

3-years Waxman-Hatch Exclusivity

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

YES ☐ NO ☒

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

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

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

YES ☐ NO ☒

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

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES ☒ NO ☐

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

NDA# 21909 Allegra (fexofenadine HCl) orally disintegrating tablet

NDA# 20872 Allegra (fexofenadine HCl) tablets

NDA# 21963 Allegra (fexofenadine HCl) oral suspension

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: Jessica M. Diaz
Title: Regulatory Project Manager
Date: 1-26-11

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

JESSICA M DIAZ
01/26/2011

ANDREA LEONARD SEGAL
01/26/2011

DEBARMENT CERTIFICATION

Sanofi-aventis 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.

Mary Beth Wigley

Mary Beth Wigley, B.S., M.S.

Assistant Director

Regulatory Research & Development Portfolio
Global Regulatory Affairs

Sanofi-aventis U.S. Inc.
on behalf of sanofi-aventis U.S. LLC

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION[1]

NDA # 201373 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type: SE6
Proprietary Name: Children's Allegra Allergy and Children's Allegra Hives Established/Proper Name: fexonfenadine HCl Dosage Form: 30mg/5ml Oral Suspension		Applicant: sanofi-aventis Agent for Applicant (if applicable): Judy Plon
RPM: Jessica M. Diaz		Division: Division of Nonprescription Clinical Evaluation

NDAs:
NDA Application Type: ☐ 505(b)(1) ☐ 505(b)(2)
Efficacy Supplement: ☒ 505(b)(1) ☐ 505(b)(2)

(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)

505(b)(2) Original NDAs and 505(b)(2) NDA supplements:
Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):

Provide a brief explanation of how this product is different from the listed drug.

If no listed drug, explain.
- ☐ This application relies on literature.
- ☐ This application relies on a final OTC monograph.
- ☐ Other (explain)

Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.

On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.

☐ No changes ☐ Updated Date of check:

If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.

❖ Actions	
• Proposed action • User Fee Goal Date is January 25, 2011	☒ AP ☐ TA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☐ None

[1] The **Application Information** section is (only) a checklist. The **Contents of Action Package** section (beginning on page 5) lists the documents to be included in the Action Package.

❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____	☐ Received
❖ Application Characteristics [2]	

Review priority: ☒ Standard ☐ Priority
Chemical classification (new NDAs only):

☐ Fast Track
☐ Rolling Review
☐ Orphan drug designation
☐ Rx-to-OTC full switch
☒ Rx-to-OTC partial switch
☐ Direct-to-OTC

NDAs: Subpart H
☐ Accelerated approval (21 CFR 314.510)
☐ Restricted distribution (21 CFR 314.520)
Subpart I
☐ Approval based on animal studies

BLAs: Subpart E
☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)
Subpart H
☐ Approval based on animal studies

☐ Submitted in response to a PMR
☐ Submitted in response to a PMC
☐ Submitted in response to a Pediatric Written Request

REMS: ☐ MedGuide
☐ Communication Plan
☐ ETASU
☐ REMS not required

Comments:

❖ BLAs only: Ensure *RMS-BLA Product Information Sheet for TBP* and *RMS-BLA Facility Information Sheet for TBP* have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)	☐ Yes, dates
❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 *(approvals only)*	☐ Yes ☐ No
❖ Public communications *(approvals only)*	
• Office of Executive Programs (OEP) liaison has been notified of action	☐ Yes ☒ No
• Press Office notified of action (by OEP)	☐ Yes ☒ No
• Indicate what types (if any) of information dissemination are anticipated	☒ None ☐ HHS Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other

[2] Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity?	☒ No ☐ Yes
• NDAs and BLAs: Is there existing orphan drug exclusivity for the "same" drug or biologic for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.*	☒ No ☐ Yes If, yes, NDA/BLA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application)? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☐ No ☐ Yes If yes, NDA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☐ No ☐ Yes If yes, NDA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☐ No ☐ Yes If yes, NDA # and date exclusivity expires:
• NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? *(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date 10-year limitation expires:
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions.	☒ Verified ☐ Not applicable because drug is an old antibiotic.
• Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.	21 CFR 314.50(i)(1)(*i*)(A) ☐ Verified 21 CFR 314.50(i)(1) ☐ (ii) ☐ (iii)
• [505(b)(2) applications] If the application includes a **paragraph III** certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).	☐ No paragraph III certification Date patent will expire
• [505(b)(2) applications] For **each paragraph IV** certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). *(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next section below (*Summary Reviews*)).*	☐ N/A (no paragraph IV certification) ☐ Verified

- [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

  Answer the following questions for **each** paragraph IV certification:

  (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification? ☐ Yes ☐ No

  (Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e))).

  *If "**Yes**," skip to question (4) below. If "**No**," continue with question (2).*

  (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)? ☐ Yes ☐ No

  *If "**Yes**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.*

  *If "**No**," continue with question (3).*

  (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant? ☐ Yes ☐ No

  (Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2))).

  *If "**No**," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.*

  (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)? ☐ Yes ☐ No

  *If "**Yes**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (*Summary Reviews*).*

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

(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification? (Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period). *If "**No**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (*Summary Reviews*).* *If "**Yes**," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.*	☐ Yes ☐ No
CONTENTS OF ACTION PACKAGE	
❖ Copy of this Action Package Checklist[3]	1/25/2011
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list *(approvals only)*	☒ Included
Documentation of consent/non-consent by officers/employees	☒ Included
Action Letters	
❖ Copies of all action letters *(including approval letter with final labeling)*	Action(s) and date(s) Approval-1/24/2011
Labeling	
❖ Package Insert *(write submission/communication date at upper right of first page of PI)*	
• Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.	Over-the-Counter Medication
• Original applicant-proposed labeling	
• Example of class labeling, if applicable	

[3] Fill in blanks with dates of reviews, letters, etc.

❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling *(write submission/communication date at upper right of first page of each piece)*	☐ Medication Guide ☐ Patient Package Insert ☐ Instructions for Use ☐ Device Labeling ☐ None
• Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.	
• Original applicant-proposed labeling	
• Example of class labeling, if applicable	
❖ Labels (**full color** carton and immediate-container labels) *(write submission/communication date on upper right of first page of each submission)*	
• Most-recent draft labeling	
❖ Proprietary Name • Acceptability/non-acceptability letter(s) *(indicate date(s))* • Review(s) *(indicate date(s))*	Acceptability Letter 12/9/2010 12/8/2010
❖ Labeling reviews *(indicate dates of reviews and meetings)*	☐ RPM ☒ DMEPA 12/13/2010 ☐ DRISK ☐ DDMAC ☐ CSS ☒ Other reviews DNRD: 12/2/2010; 12/15/2010; 1/13/2011; Labeling Meeting: 1-6-2011
Administrative / Regulatory Documents	
❖ Administrative Reviews *(e.g., RPM Filing Review[4]/Memo of Filing Meeting) (indicate date of each review)* ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment *(indicate date)*	11/26/2010 ☒ Not a (b)(2) ☒ Not a (b)(2)
❖ NDAs only: Exclusivity Summary *(signed by Division Director)*	☒ Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
• Applicant is on the AIP	☐ Yes ☒ No
• This application is on the AIP o If yes, Center Director's Exception for Review memo *(indicate date)* o If yes, OC clearance for approval *(indicate date of clearance communication)*	☐ Yes ☒ No ☐ Not an AP action
❖ Pediatrics *(approvals only)* • Date reviewed by PeRC _____ If PeRC review not necessary, explain: _____ • Pediatric Page/Record *(approvals only, must be reviewed by PERC before finalized)*	☐ Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent *(include certification)*	☒ Verified, statement is acceptable

[4] Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

❖ Outgoing communications *(letters (except action letters), emails, faxes, telecons)*	5/3, 6/21, 7/1, 9/17, 9/23, 10/7, 10/22, 11/22, and 11/22/2010
❖ Internal memoranda, telecons, etc.	11/23/2010 - Office Level Internal Meeting
❖ Minutes of Meetings	
• Regulatory Briefing *(indicate date of mtg)*	☒ No mtg
• If not the first review cycle, any end-of-review meeting *(indicate date of mtg)*	☒ N/A or no mtg
• Pre-NDA/BLA meeting *(indicate date of mtg)*	☒ No mtg
• EOP2 meeting *(indicate date of mtg)*	☒ No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) *(indicate dates of mtgs)*	N/A
❖ Advisory Committee Meeting(s)	☒ No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available *(do not include transcript)*	
Decisional and Summary Memos	
❖ Office Director Decisional Memo *(indicate date for each review)*	☒ None
Division Director Summary Review *(indicate date for each review)*	☐ None 1/22/2011
Cross-Discipline Team Leader Review *(indicate date for each review)*	☐ None 12/21/2010
PMR/PMC Development Templates *(indicate total number)*	☐ None
Clinical Information[5]	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) *(indicate date for each review)*	12/21/2010
• Clinical review(s) *(indicate date for each review)*	12/2/2010 DNCE; 11/23/2010 DPARP
• Social scientist review(s) (if OTC drug) *(indicate date for each review)*	☒ None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here ☐ and include a review/memo explaining why not *(indicate date of review/memo)*	
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers *(indicate date of each review)*	☒ None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation *(indicate date of each review)*	☒ Not applicable
❖ Risk Management • REMS Documents and Supporting Statement *(indicate date(s) of submission(s))* • REMS Memo(s) and letter(s) *(indicate date(s))* • Risk management review(s) and recommendations (including those by OSE and CSS) *(indicate date of each review and indicate location/date if incorporated into another review)*	☒ None
❖ DSI Clinical Inspection Review Summary(ies) *(include copies of DSI letters to investigators)*	☒ None requested

[5] Filing reviews should be filed with the discipline reviews.

Clinical Microbiology ☒ None	
❖ Clinical Microbiology Team Leader Review(s) *(indicate date for each review)*	☐ None
Clinical Microbiology Review(s) *(indicate date for each review)*	☐ None
Biostatistics ☒ None	
❖ Statistical Division Director Review(s) *(indicate date for each review)*	☐ None
Statistical Team Leader Review(s) *(indicate date for each review)*	☐ None
Statistical Review(s) *(indicate date for each review)*	☐ None
Clinical Pharmacology ☐ None	
❖ Clinical Pharmacology Division Director Review(s) *(indicate date for each review)*	☒ None
Clinical Pharmacology Team Leader Review(s) *(indicate date for each review)*	☒ None
Clinical Pharmacology review(s) *(indicate date for each review)*	☐ None 11/22/2010; 1/7/2011
❖ DSI Clinical Pharmacology Inspection Review Summary *(include copies of DSI letters)*	☒ None
Nonclinical ☐ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) *(indicate date for each review)*	☒ None
• Supervisory Review(s) *(indicate date for each review)*	☒ None
• Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	☐ None 11/23/2010
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer *(indicate date for each review)*	☒ None
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	☒ No carc
❖ ECAC/CAC report/memo of meeting	☒ None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary *(include copies of DSI letters)*	☒ None requested
Product Quality ☐ None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) *(indicate date for each review)*	☒ None 1/21/2011 Memorandum
• Branch Chief/Team Leader Review(s) *(indicate date for each review)*	☒ None
• Product quality review(s) including ONDQA biopharmaceutics reviews *(indicate date for each review)*	☐ None 12/21/2010
❖ Microbiology Reviews ☐ NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) *(indicate date of each review)* ☐ BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) *(indicate date of each review)*	☒ Not needed
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer *(indicate date of each review)*	☒ None

❖ Environmental Assessment (check one) (original and supplemental applications)	
☒ Categorical Exclusion *(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)*	11/22/10; 12/22/2010 CMC Review Page 10 of 10.
☒ Review & FONSI *(indicate date of review)*	11/30/2010
☐ Review & Environmental Impact Statement *(indicate date of each review)*	
❖ Facilities Review/Inspection	
☒ NDAs: Facilities inspections (include EER printout) *(date completed must be within **2 years** of action date) (only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites[6])*	Date completed: CMC Memorandum 1-21-2011 ☒ Acceptable ☐ Withhold recommendation ☐ Not applicable
☐ BLAs: TB-EER *(date of most recent TB-EER must be within **30 days** of action date) (original and supplemental BLAs)*	Date completed: ☐ Acceptable ☐ Withhold recommendation
❖ NDAs: Methods Validation *(check box only, do not include documents)*	☐ Completed ☐ Requested ☐ Not yet requested ☒ Not needed (per review)

[6] I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Appendix to Action Package Checklist

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

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

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

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

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

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

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

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

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

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/s/

JESSICA M DIAZ
01/26/2011

From: Rothman, Barry
Sent: Friday, January 21, 2011 3:43 PM
To: Leonard Segal, Andrea; Schiffenbauer, Joel; Ganley, Charles J; Furness, Melissa; Nasr, Moheb M; Diaz, Jessica M; Ocheltree, Terrance
Cc: Rosa, Carmelo R; Campbell, Douglas (CDER); Friedman, Rick L; Cruz, Concepcion
Subject: RE: NDA 201613 General Review (REV-QUALITY-03)

Andrea,

Yes, the language applies to the efficacy supplements for NDA 21-909 S003, NDA 20-786 S027 and NDA 21-704 S008.

Barry

Barry Rothman
Chief
Manufacturing Assessment and Preapproval
Compliance Branch
Division of Manufacturing and Product Quality
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration

From: Rothman, Barry
Sent: Friday, January 21, 2011 2:57 PM
To: Schiffenbauer, Joel; Ganley, Charles J; Furness, Melissa; Nasr, Moheb M; Diaz, Jessica M; Ocheltree, Terrance; Leonard Segal, Andrea
Cc: Rosa, Carmelo R; Campbell, Douglas (CDER); Friedman, Rick L
Subject: NDA 201613 General Review (REV-QUALITY-03)

Folks,

We consider the Sanofi Aventis Deutschland GmbH facility to be acceptable for the manufacture of APIs referenced in NDAs 201613 and 201373:

The most recent FDA inspection of the Sanofi Aventis Deutschland GmbH facility, conducted during September 2010, did not observe significant cGMP violations involving the manufacture or testing of the API, fexofenadine. The API manufacturing operations are conducted in a separate facility and under a separate QA and management structure from that used for sterile drug manufacturing. Although we continue to have concerns regarding the firm's sterile drug manufacturing operations, none of the sterile drug product issues are related to the manufacture of APIs. (b) (4)

Barry

Barry Rothman
Chief
Manufacturing Assessment and Preapproval
Compliance Branch
Division of Manufacturing and Product Quality
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration

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/s/

MELISSA H FURNESS
01/23/2011

Furness, Melissa

From: Katz, Donna
Sent: Thursday, January 13, 2011 9:10 AM
To: Furness, Melissa; Dettelbach, Kim
Cc: Leonard Segal, Andrea; Schiffenbauer, Joel; Shetty, Daiva
Subject: RE: NDAs 20-786/SE-027, 21-704/SE-008, 21-909/SE-003, 201-613, 201-373 (Allegra Switch Applications)

Melissa,

Kim and I have reviewed the materials, and it doesn't appear to us that this application triggers PREA.

Donna and Kim

From: Furness, Melissa
Sent: Thursday, January 06, 2011 2:27 PM
To: Dettelbach, Kim; Katz, Donna
Cc: Leonard Segal, Andrea; Schiffenbauer, Joel; Shetty, Daiva
Subject: FW: NDAs 20-786/SE-027, 21-704/SE-008, 21-909/SE-003, 201-613, 201-373 (Allegra Switch Applications)

Hi Kim and Donna,

We need your help. We would greatly appreciate your assitance as our PDUFA dates for the above referenced applications are fast approaching, and we wish to have confirmation that our conclusions are correct. We have previously contacted PMHS, but have not received a final decision from them. We do not believe that the above referenced Allegra switch applications trigger PREA. Can you please provide us with your opinion regarding our conclusions. I am attaching the pertinent information that we believe supports our conclusions.

<< File: cover.pdf >> << File: ped-waiver.pdf >> << File: Meeting minutes 12_09.pdf >> << File: NDA 21634 acknowledge letter_no under 12.pdf >> << File: PMHS acceptance of exemption for -D products 2007.pdf >>
Please let me know if you require any additional information.

Thanks in advance for your time.

Melissa

Melissa Hancock Furness
Chief, Project Management Staff
FDA/CDER/OND/ODE IV/DNCE

phone: 301-796-0893
e-mail: Melissa.Furness@fda.hhs.gov

From: Furness, Melissa
Sent: Monday, January 03, 2011 2:40 PM
To: Addy, Rosemary
Cc: Diaz, Jessica M; Shetty, Daiva; Leonard Segal, Andrea; Schiffenbauer, Joel; Mathis, Lisa; Furness, Melissa
Subject: RE: NDAs 20-786/SE-027, 21-704/SE-008, 21-909/SE-003, 201-613, 201-373 (Allegra Switch Applications)

Hi Rosemary,

Happy New Year. I wanted to touch base to see if you have any updates for us regarding our below inquiry.

Thanks,

Melissa

From: Furness, Melissa
Sent: Thursday, December 09, 2010 11:26 AM
To: Addy, Rosemary
Cc: Diaz, Jessica M; Shetty, Daiva; Leonard Segal, Andrea; Schiffenbauer, Joel; Mathis, Lisa; Raffaelli, Ryan; Hu, Linda S
Subject: RE: NDAs 20-786/SE-027, 21-704/SE-008, 21-909/SE-003, 201-613, 201-373 (Allegra Switch Applications)

Rosemary,

Here is some pertinent information that we pulled from the EDR and DARRTS for you.

<< File: cover.pdf >> << File: ped-waiver.pdf >> << File: Meeting minutes 12_09.pdf >> << File: NDA 21634 acknowledge letter_no under 12.pdf >> << File: PMHS acceptance of exemption for -D products 2007.pdf >>
Thanks,

Melissa

From: Addy, Rosemary
Sent: Thursday, December 09, 2010 9:58 AM
To: Furness, Melissa
Cc: Diaz, Jessica M; Shetty, Daiva; Leonard Segal, Andrea; Schiffenbauer, Joel; Mathis, Lisa
Subject: RE: NDAs 20-786/SE-027, 21-704/SE-008, 21-909/SE-003, 201-613, 201-373 (Allegra Switch Applications)

Hi Melissa,

Unfortunately, this seems to be a case similar to the one you sent me abou (b) (4). You have not given me sufficient information to answer your question. It is not possible to answer these questions in a vacuum. In order for me to answer your question, you will need to send me additional information, including the sponsor's rationale/justification. If I am going to comment on your conclusions, I need to have the same information that you had when reaching those conclusions.

Thanks.
Rosemary

From: Furness, Melissa
Sent: Wednesday, December 08, 2010 8:57 PM
To: Addy, Rosemary
Cc: Diaz, Jessica M; Shetty, Daiva; Leonard Segal, Andrea; Schiffenbauer, Joel
Subject: NDAs 20-786/SE-027, 21-704/SE-008, 21-909/SE-003, 201-613, 201-373 (Allegra Switch Applications)

Hi Rosemary,

The sponsor for the above referenced applications submitted a rationale/justification as to why they believe these applications do not trigger PREA. The review team agreed with the sponsors assertion that these applications do not trigger PREA as they do not involve a new active ingredient, dosage form, indication, route of administration or dosing regimen. We wanted to mention this decision to PMHS. Please let us know if you disagree with our conclusions.

Thanks and have a nice evening,

Melissa

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/s/

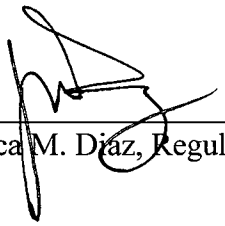
MELISSA H FURNESS
01/20/2011

Refer to CMC review for Dissolution and Stability.

Jessica M. Diaz, Regulatory Project Manager

Date: 12-17-10

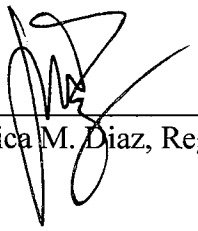
No P/T consult were generated during this review.



Jessica M. Diaz, Regulatory Project Manager

Date: 12.17.10

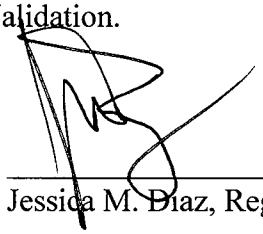
Refer to CMC review for EER.



Jessica M. Diaz, Regulatory Project Manager

Date: 12.17.10

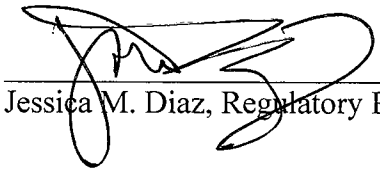
Refer to CMC review for Methods Validation.



Jessica M. Diaz, Regulatory Project Manager

Date: 12.17.10

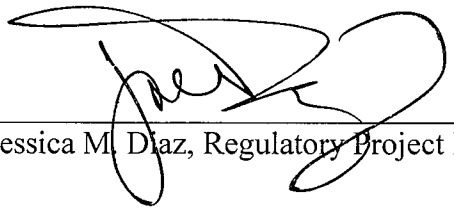
Refer to DARRTS record for incoming regulatory submissions.



Jessica M. Diaz, Regulatory Project Manager

Date: 12·13·2010

The Sponsor was not on the AIP List.



Jessica M. Diaz, Regulatory Project Manager

Date: 12·13·2010

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 201373
NDA 201613
NDA 021909/S-003

PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE

Sanofi-Aventis U.S. LLC
9 Great Valley Parkway
P.O. Box 3026, GV31-123
Malvern, PA 19355

ATTENTION: Mary Beth Wigley, B.S., M.S.
Assistant Director, Regulatory R&D Portfolio, Global Regulatory Affairs

Dear Ms. Wigley:

Please refer to your New Drug Applications (NDA) and supplemental New Drug Application (sNDA) dated March 25, 2010, received March 25, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fexofenadine Hydrochloride Oral Suspension, 30 mg/5 mL (NDA 201373), Fexofenadine Hydrochloride Tablets, 30 mg, 60 mg, and 180 mg (NDA 201613), and Fexofenadine Hydrochloride Orally Disintegrating Tablets, 30 mg (NDA 021909/S-003).

We also refer to your May 13, 2010, correspondence, received May 14, 2010, and submitted to each of the above referenced applications, requesting review of your proposed proprietary names as follows:

NDA	Dosage Form/Strength	Proposed Proprietary Name(s)
201373	Fexofenadine Hydrochloride Oral Suspension, 30 mg/ 5 mL	Children's Allegra Allergy and Children's Allegra Hives
[redacted]	[redacted]	(b) (4)
021909/S-003	Fexofenadine Hydrochloride orally disintegrating tablets, 30 mg	Children's Allegra Allergy and Children's Allegra Hives

We have completed our review of the proposed proprietary names for each product and strength and have concluded that these proposed proprietary names are acceptable.

If **any** of the proposed product characteristics as stated in your May 13, 2010 NDA and supplemental NDA submissions are altered prior to approval of the marketing applications, the proprietary name for that specific NDA or supplemental NDA should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Janet Anderson, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0675. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Jessica Diaz at (301) 796-4908.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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/s/

DENISE P TOYER on behalf of CAROL A HOLQUIST
12/09/2010

MEMORANDUM OF MEETING MINUTES

MEETING DATE:	October 25, 2010
TIME:	12:00 – 1:00 P.M.
LOCATION:	CDER WO Conference Room 1415, Bldg 22
APPLICATION(S):	NDA(s) 21909 S-003; 201613; 201373; 20786 S-027; 21704 S-008
DRUG NAME:	Allegra® (fexofenadine) ODT 30mg Allegra® (fexofenadine) tablets 30, 60, 180mg Allegra® (fexofenadine) oral suspension 30mg/5ml Allegra-D® 12-hour (fexofenadine HCl 60mg/ pseudophedrine HCl 120mg) ER tablets Allegra-D® 24-hour (fexofenadine HCl 180mg/ pseudophedrine HCl 240mg) ER tablets
TYPE OF MEETING:	Internal meeting
MEETING CHAIR:	Dr. Andrea Leonard-Segal, M.D.
MEETING RECORDER:	Jessica M. Diaz, R.N., B.S.N., M.S.H.S.

FDA ATTENDEES:

Office of Drug Evaluation IV
Charles J. Ganley, M.D., Director
Shaw T. Chen, M.D., Deputy Director

Division of Nonprescription Clinical Evaluation (DNCE)
Andrea Leonard-Segal, M.D., Director
Joel Schiffenbauer, M.D., Deputy Director
Daiva Shetty, M.D., Medical Team Leader
Linda Hu, M.D., Medical Officer
Melissa Hancock Furness, Chief, Project Management Staff
LCDR Jessica M. Diaz, R.N., M.S.H.S., Regulatory Project Manager

Office of Drug Evaluation II
Curtis J. Rosebraugh, M.D., Deputy Director

Division of Pulmonary and Rheumatological Products (DPRP)
Badrul A. Chowdhury, M.D., Director
Sally M. Seymour, M.D., Deputy Director Safety
Theresa M. Michele, M.D., Medical Team Leader

Office of Drug Evaluation I
Ellis F. Unger, M.D., Deputy Director

Division of Cardiology and Renal Products (DCRP)
Norman Stockbridge, M.D., Ph.D., Director
Suchitra Balakrishnan, M.D., Clinical Reviewer
Hao Zhu, M.D., Clinical Reviewer, Fellow

Office of Medical Policy
Robert Temple, M.D., Director

EXTERNAL CONSTITUENT ATTENDEES:

None

BACKGROUND:

The sponsor submitted five NDAs for a prescription (Rx) to nonprescription switch for the Allegra mono-ingredient and the Allegra combination-ingredient products on March 26, 2010. The Division of Nonprescription Clinical Evaluation (DNCE) submitted a consult to the Division of Cardiovascular and Renal Products (DCRP) on April 8, 2010 to evaluate the ECG and cardiac adverse event data as part of the safety evaluation of fexofenadine for the Rx-to-OTC switch applications. A TQT study had not been previously performed for fexofenadine, but there is a vast pre-and post-marketing clinical safety database for this active ingredient. The consult request stated:

"Sanofi Aventis has submitted applications for the Rx-to-OTC switch of fexofenadine (Allegra) tablets, oral disintegrating tablets, and oral suspension (NDA 201-613, 201-373 and 21-909). We are reexamining the safety profile of fexofenadine as part of the switch applications. The NDA submissions include an analysis of ECGs obtained in clinical studies submitted for previously approved fexofenadine NDAs, in addition to new ECG data not previously submitted to the FDA. The analyses include the evaluation of changes of ECG parameters from baseline and frequencies of potentially clinically significant ECG changes.

We are consulting with you to evaluate the ECG data and cardiac adverse event data (especially post-marketing data--see section 6 in the ISS starting on p.107 and cardiac adverse event information in the Adverse Events of Special Interest section of the Postmarketing Report) for the 2 new NDAs and the 1 efficacy supplement. The safety data analysis, presented in the ISS (section 5.3.5.3) of these three submissions, is identical. Please review and advise if there are cardiac safety concerns with fexofenadine."

DCRP's consult concluded that fexofenadine is unlikely to be associated with large changes in QTc interval; however, all available clinical trials appear to be inadequate to rule out small effects on QTc interval (<10 ms). Therefore, DCRP recommended that the sponsor conduct a TQT study prior to OTC conversion.

The DCRP consult recommendation will impact the over-the-counter (OTC) switch NDAs for Allegra-D 12 hour and Allegra-D 24 hour products currently under review. Additionally, it impacts the other 2nd generation antihistamines that are OTC (e.g., loratadine and cetirizine) and

prescription and may even impact some first generation antihistamines. DNCE scheduled this internal meeting so that relevant members of upper management could consider the clinical basis for DCRPs recommendation and provide a recommendation as to the appropriate next steps.

MEETING OBJECTIVES:

To determine the need for TQT study for fexofenadine.

DISCUSSION POINTS:

1. DCRP stated that the decision regarding the request for a TQT study is based on all the available clinical trials, which appear to be inadequate to rule out small effects on QTc interval (<10 ms) as defined by ICH E14 guidance.
2. The Office of Surveillance and Epidemiology's (OSE) review in 2000 found the evidence inconclusive to establish a direct association between fexofenadine and cardiac events. The OSE review completed on October 8, 2010 did not identify new safety issues with fexofenadine regarding QT prolongation and Torsade de Pointes.
3. All the previously approved OTC antihistamines were developed at the time when QT guidance was not available. There is no difference in the number of postmarketing cardiac events reported among fexofenadine, loratadine, or cetirizine.
4. There were no cardiac cases for fexofenadine reported during the drug development phase. This was not the situation for the three drugs that have been withdrawn from the market due to QT prolongation; there were cases reported in clinical trials for these drugs.
5. If we request the sponsor to conduct a TQT study by the current standards, and they see a 5 msec change in QT, a regulatory decision may not be different. This would not likely impact on the decision to make the drug available OTC.
6. Overall, many meeting participants agreed that there is no study available for QT assessment based on current standards; however, data available from clinical trials and postmarketing are sufficient to address the concerns with QT prolongation.
7. Since there is internal disagreement within the Agency, Dr. Temple recommended the reviewers in DCRP reconvene to re-review all the available data and that they reconsider their recommendation. After they re-review the information they should provide a substantive rationale to justify their conclusion and recommendation. For example, they should address whether a finding a small QT prolongation would change our regulatory decision (e.g., would it change our view of the clinical safety of the drug?)

DECISIONS (AGREEMENTS) REACHED:

DCRP reviewers will re-convene and review the data submitted by Sanofi-aventis and any available additional data on ECG data for other products of this class.

UNRESOLVED ISSUES OR ISSUES REQUIRING FURTHER DISCUSSION:

The recommendation to request a TQT study is still pending follow-up review from DCRP.

ACTION ITEMS:

Record this decision as internal meeting minutes.

ATTACHMENTS/HANDOUTS:

None

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JESSICA M DIAZ
11/23/2010

From: Diaz, Jessica M
Sent: Monday, November 22, 2010 12:51 PM
To: 'Judy.Plon@sanofi-aventis.com'
Subject: Allegra Single-Ingredient Product Information Request

Importance: High

Good morning Judy,

Please see below a request from the Clinical Reviewer for the Allegra Single Ingredient Products. We need a response as soon as possible, this is time sensitive.

Call me if you have any questions.

Please:

- Clarify, why the number of countries where Allegra is non-prescription differs from one submission to another? (excerpts below for #1-3)
- Provide the number and a list of the countries where Allegra is marketed for nonprescription use
- Provide, where Allegra has been available without a prescription for over 10 years

1) The summary of clinical safety states: "They have been approved and available without a prescription in approximately 13 countries for over 10 years." P 11

2) The safety update states: "fexofenadine hydrochloride was first approved for over-the-counter use in Canada in June 1997 (Allegra 12 Hour®, 60 mg twice daily). Since that time, it has been approved in 7 additional countries for OTC use: Belgium, Mexico, Republic of Moldova, Netherlands, New Zealand, Russian Federation and Uzbekistan. Additionally, the once-daily 120 mg formulation (Allegra 24 Hour®) was also approved in Canada in October 2000." P 51

3) Your October 14th response to an information request on labeling and where the product is marketed OTC listed 22 countries where the product is marketed as a nonprescription drug product.

Jess

LCDR Jessica M. Diaz, RN, BSN, MSHS
United States Public Health Services
Regulatory Project Manager
FDA-CDER-ODE IV
Division of Nonprescription Clinical Evaluation
10903 New Hampshire Avenue, Bldg. 22, Room 5483
Silver Spring, MD 20993
Office: 301-796-4908 Fax: 301-796-9899
Email: Jessica.Diaz@fda.hhs.gov

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/s/

JESSICA M DIAZ
11/22/2010

From: Diaz, Jessica M
Sent: Friday, November 19, 2010 3:56 PM
To: 'Judy.Plon@sanofi-aventis.com'
Subject: Allegra Single Ingredient Products Information Request

Good afternoon Judy,

Please see below a request from the Clinical Reviewer regarding the Allegra single-ingredient products.

What data was used to support the following language found in the Netherlands and harmonized EU Patient Leaflet?

(b) (4)

[redacted]

Please contact me if you have any questions.

Best regards,

Jess

LCDR Jessica M. Diaz, RN, BSN, MSHS
United States Public Health Services
Regulatory Project Manager
FDA-CDER-ODE IV
Division of Nonprescription Clinical Evaluation
10903 New Hampshire Avenue, Bldg. 22, Room 5483
Silver Spring, MD 20993
Office: 301-796-4908 Fax: 301-796-9899
Email: Jessica.Diaz@fda.hhs.gov

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/s/

JESSICA M DIAZ
11/22/2010

From: Diaz, Jessica M
Sent: Friday, October 22, 2010 2:21 PM
To: 'Judy.Plon@sanofi-aventis.com'
Cc: Diaz, Jessica M
Subject: Allegra-D and Allegra NDAs Information Request

Good afternoon Judy:

We have an Information Request from our Clinical Pharmacology Reviewers regarding the Allegra products. See below:

"Please provide drug interactions study report along with supporting data for the study done with fexofenadine hydrochloride and aluminum and magnesium containing antacids".

Please contact me if you have any questions.

Best regards,

Jess

LCDR Jessica M. Diaz, RN, BSN, MSHS
United States Public Health Services
Regulatory Project Manager
FDA-CDER-ODE IV
Division of Nonprescription Clinical Evaluation
10903 New Hampshire Avenue, Bldg. 22, Room 5483
Silver Spring, MD 20993
Office: 301-796-4908 Fax: 301-796-9899
Email: Jessica.Diaz@fda.hhs.gov

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/s/

JESSICA M DIAZ
10/22/2010

From: Diaz, Jessica M
Sent: Thursday, October 07, 2010 10:09 AM
To: 'Judy.Plon@sanofi-aventis.com'
Cc: Diaz, Jessica M
Subject: Information Request for Allegra Single Ingredient Products NDA 21909/S-003; NDA 201613; NDA 201373

Importance: High

Good morning Judy,

See below an information request from our Clinical and Labeling Reviewer for the Allegra single-ingredient products.

Provide a table listing of all foreign countries where the single ingredient Allegra product is marketed or withdrawn from market place, as a nonprescription, the date of initial approval or withdrawal , the approved dosage strengths and if a patient leaflet is /was handed out with the nonprescription drug products. For the withdrawn products, the reason of withdrawal. This table should be organized by country and then by dosage strength, date of approval /withdrawal. reason for withdrawal and whether or not a patient leaflet is provided. This table listing should be submitted for the following applications: 201-373, 201-613 and 21-909.

Thank you and have a good day!

Jess

LCDR Jessica M. Diaz, RN, BSN, MSHS
United States Public Health Services
Regulatory Project Manager
FDA-CDER-ODE IV
Division of Nonprescription Clinical Evaluation
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/s/

JESSICA M DIAZ
10/07/2010

From: Diaz, Jessica M
Sent: Thursday, September 23, 2010 9:14 AM
To: 'Judy.Plon@sanofi-aventis.com'
Cc: Diaz, Jessica M
Subject: Information Request for Allegra NDAs 201613; 201373; 21909 S-003 and Allegra-D NDAs 21704 S-008 and 20786 S-027

Good Morning Judy,

In our review of the labeling there is additional information we need to facilitate the process. The labeling reviewer and clinical reviewer request the following information for the Allegra and Allegra-D products. Please provide a response as soon as possible to facilitate the review of the materials requested.

Information Request:

Provide a complete listing of all SKU's (with respective count sizes) for the mono-ingredient and combination-ingredient drug products. In addition, please confirm the date of the most recent submission of all SKU's.

Provide the English translation of the foreign nonprescription carton labels for NDA 201-613. We acknowledge the receipt of the translated English leaflets for some of the non-translated foreign carton labels however we are specifically interested reviewing the nonprescription carton labels in English.

Thank you,

Jess

Jessica M. Diaz, LCDR, USPHS
Regulatory Project Manager
FDA-CDER-ODE IV
Division of Nonprescription Clinical Evaluation
10903 New Hampshire Avenue, Bldg. 22, Room 5483
Silver Spring, MD 20993
Office: 301-796-4908 Fax: 301-796-9899
Email: Jessica.Diaz@fda.hhs.gov

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/s/

JESSICA M DIAZ
09/23/2010

From: Diaz, Jessica M
Sent: Tuesday, June 29, 2010 1:23 PM
To: 'Mary-Beth.Wigley@sanofi-aventis.com'
Subject: NDA 201613; NDA 201373; NDA21909/ S003: Follow-Up re: T-Con June 28, 2010

Attachments: Allegra NDA 201613-201373-21909 Table Sample.pdf

Mary-Beth:

As promised I am sending you an electronic record of the information request that we communicated to you verbally during our 9 AM telephone conversation. Please see below specific comments relevant to the teleconference.

A) The way the documents are hyperlinked in Module 2.7 are adequate for the reviewer. This method can be used for the requested table.
B) Please submit the table summarizing all 134 studies with revisions as noted in the PDF attachment.

As an additional information request please submit for review study M01455A/4136

Please provide a timeline for the submissions requested.

Thank you.

Best regards,

Jess

Allegra NDA
)1613-201373-2190

LCDR Jessica M. Diaz, RN, BSN, MSHS
United States Public Health Services
Regulatory Health Project Manager
FDA-CDER-ODE IV
Division of Nonprescription Clinical Evaluation
10903 New Hampshire Avenue, Bldg. 22, Room 5483
Silver Spring, MD 20993
Office: 301-796-4908 Fax: 301-796-9850
Email: Jessica.Diaz@fda.hhs.gov

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/s/

JESSICA M DIAZ
09/17/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021909 S-003
NDA 201613
NDA 201373
NDA 020786 S-027
NDA 021704 S-008

MEETING DENIED

sanofi-aventis, U.S., LLC
Attention: Mary-Beth Wigley, B.S., M.S.
Assistant Director, Regulatory R & D Portfolio,
Global Regulatory Affairs
9 Great Valley Parkway
P.O. Box 3026, GV31-123
Malvern, PA 19355

Dear Ms. Wigley:

Please refer to your March 25, 2010, supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for ALLEGRA®, (fexofenadine HCl), orally disintegrating tablets 30mg, ALLEGRA®, (fexofenadine HCl), tablets, 30, 60, and 180 mg, ALLEGRA®, (fexofenadine HCl), oral suspension, 30mg/5ml, ALLEGRA-D 12-Hour, (fexofenadine HCl 60mg and pseudoephedrine HCl 120mg), extended-release tablets, ALLEGRA-D 24-Hour, (fexofenadine HCl (b) (4) mg and pseudoephedrine HCl 240mg), extended-release tablets.

We also refer to your July 22, 2010, correspondence requesting a meeting to obtain FDA feedback on your proposed labeling and your efforts to address the potential for consumer confusion regarding the two dosage strengths. We are denying the meeting request because it is too early in the review cycle to discuss labeling review findings for these applications. As stated in our filing letters of June 7, 2010, if major deficiencies are not identified during the review, we plan to discuss your proposed labeling by December 17, 2010. No formal meeting request is necessary to initiate this portion of the review process.

If you have any questions, call Jessica M. Diaz, Regulatory Project Manager at (301) 796-4908.

Sincerely,

{See appended electronic signature page}

Melissa H. Furness
Chief, Project Management Staff
Division of Nonprescription Clinical Evaluation
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21704	GI-1	SANOFI AVENTIS US LLC	ALLEGRA-D 24 HOUR(FEXOFENADINE/PSEUDOEPH
NDA-20786	GI-1	SANOFI AVENTIS US LLC	ALLEGRA D
NDA-21909	GI-1	SANOFI AVENTIS US LLC	ALLEGRA (FEXOFENADINE HCL)
NDA-201373	GI-1	SANOFI AVENTIS US LLC	FEXOFENADINE HCL
NDA-201613	GI-1	SANOFI AVENTIS US LLC	Allegra (Fexofenadine Hcl) oral tablets

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/s/

MELISSA H FURNESS
08/04/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Office/Division)*: Raanan (Ron) Bloom, OPS/PARS, 301-796-2185

FROM (*Name, Office/Division, and Phone Number of Requestor)*: Youbang Liu 301-796-1926 or Jeannie David 301-796-4247
Office of New Drug Quality Assessment

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
July 16, 2010		201,373	NDA original submission	3/25/2010

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
FEXOFENADINE HCL	Standard review		9/25/2010

NAME OF FIRM: SANOFI AVENTIS US LLC

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE / ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END-OF-PHASE 2a MEETING
- ☐ END-OF-PHASE 2 MEETING
- ☐ RESUBMISSION
- ☐ SAFETY / EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☒ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

- ☐ PRIORITY P NDA REVIEW
- ☐ END-OF-PHASE 2 MEETING
- ☐ CONTROLLED STUDIES
- ☐ PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):
- ☐ CHEMISTRY REVIEW
- ☐ PHARMACOLOGY
- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE 4 STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL - BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG SAFETY

- ☐ PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ NONCLINICAL

COMMENTS / SPECIAL INSTRUCTIONS: This is a new NDA for Allegra (fexofenadine HCl) oral suspension 30mg/5mL. An environmental assessment report is included in the NDA. The NDA is electronic (in EDR). Please notify me of the assigned reviewer.

SIGNATURE OF REQUESTOR	METHOD OF DELIVERY (Check one)
{see electronic signature}	☐ DFS ☒ EMAIL ☐ MAIL ☐ HAND
PRINTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201373	ORIG-1	SANOFI AVENTIS US LLC	FEXOFENADINE HCL

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/s/

JEANNIE C DAVID
07/16/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 201-373 **INFORMATION REQUEST**

sanofi-aventis, U.S., LLC
Attention: Mary-Beth Wigley, B.S., M.S.
Assistant Director, Global Regulatory Affairs
9 Great Valley Parkway
P.O. Box 3026, GV31-123
Malvern, PA 19355

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 HCl) oral suspension, 30 mg/5 mL.

We are reviewing the CMC section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA. Please provide your response by (July 30, 2010).

1. Provide a sample of the drug product in the to-be-marketed container closure system, including dosing cup.

2. Provide validation data to support the accuracy and precision of dosing using the proposed dosing cup. Information regarding the maximum volume capacity for the dosing cup should be included in your response.

3. Provide a detailed dimensional drawing for the dosing cup (e.g., size of markings, placement of graduations, wall thickness, etc.), a copy of the supplier's certificate of analysis, and clarify which critical dimensions are inspected by the applicant as part of the incoming test specifications for release of the dosing cup for drug product manufacturing.

4. At a minimum, a specific identity test must be performed on each packaging component for the drug product immediate container/closure system. Identity test data from the supplier’s certificate of analysis may not be accepted in lieu of such testing by the drug product manufacturer. Provide revised specification tables indicating the specific identity test and acceptance criterion, including methodology, to be performed on all packaging components (e.g, IR and physical appearance)

5. Update the drug product stability data to include, minimally, 6 months’ data for each configuration studied.

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to both Youbang Liu, Regulatory Health Project Manager in the Office of New Drug Quality Assessment (Youbang.Liu@fda.hhs.gov), and Jessica Diaz, Regulatory Health Project Manager the Office of New Drugs (Jessica.Diaz@fda.hhs.gov).

If you have any questions, please call Youbang Liu, Regulatory Project Manager, at (301) 796-1926.

Sincerely,

{See appended electronic signature page}

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201373	ORIG-1	SANOFI AVENTIS US LLC	FEXOFENADINE HCL

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/s/

MOO JHONG RHEE
07/15/2010
Chief, Branch IV

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADM NISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:	FROM:
OSE **Catherine Carr, RPM**	Jessica Diaz, RPM ODEIV - DIVISION OF NON-PRESCRIPTION CLINICAL EVALUATION Tel #: 6-4908

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
6-21-2010		201613; 201373; sNDA 21-909 S-003	2 New NDAs and 1 efficacy supplement	March 26, 2010

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Allegra	High	antihistamine	September 30, 2010

NAME OF FIRM: Sanofi-Aventis

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ 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
- X☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY 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
- X☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- X☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Sanofi Aventis has submitted applications for the Rx-to-OTC switch of fexofenadine (Allegra) tablets, oral disintegrating tablets, and oral suspension (NDA 201-613, 201-373 and 21-909). We are evaluating fexofenadine post-marketing data as part of the safety profile assessment for the switch applications.

Please review AERS for serious cardiac adverse events including ventricular arrhythmias, deaths, drug interactions, and hepatic events associated with fexofenadine. The Sponsor's **data-mining analysis** of the FDA AERS database obtained through the Freedom of Information (FOI) was performed using (b) (4). The spontaneous reports with fexofenadine entered by the FDA from 1 February 1969 (the beginning of the FDA AERS database) to 30 June 2009 were included in these analyses. A similar analysis was performed using (b) (4) on the WHO UMC database, covering spontaneous reports from 01 January 1967 (the beginning of the WHO UMC database) to 31 September 2009.

The **AERS** EBGM analyses by MedDRA high level group term (HLGT) revealed a safety signal for fexofenadine

and comparators. Safety signals for fexofenadine with EBGM 05 ≥ 2.0 include cardiac arrhythmias as well as cardiac and vascular investigations associated with fexofenadine and loratadine. The submission states that further evaluation at the MedDRA preferred term (PT) level revealed that QT prolongation and Torsades de Pointes (TdP) were potential signals. The analyses by MedDRA HLGT also revealed a signal for hepatic and hepatobiliary disorders with fexofenadine and loratadine. The signals of gastrointestinal tract disorders congenital and cardiac and vascular disorders congenital were identified with fexofenadine as well.

We request that you evaluate the results of the EBGM analyses of AERS reports, emphasizing the cardiac and hepatic safety signals. For your convenience, the discussion of post-marketing adverse event data starts on p.108 of the main ISS for NDA 201,613 (Section 6) and the Postmarketing Report starts on p. 10694 in the ISS, Appendix 17. Please note therein particularly Section 7 Adverse Events of Special Interest (p. 10777).

The Sponsor provides further discussion of the AERS data mining in the Report of External Database Analyses, starting p. 24992 in Appendix 17. Table 4 below is reproduced from that report. More detailed results of the disproportionality analysis are in Appendix II, starting on p. 25036.

Table 4 – Signals of SAEs by MedDRA HLGT (EBGM 05 ≥2.0) for Fexofenadine and Comparators in the FDA AERS Database

Drugs	SAEs by MedDRA HLGT	Observed Count	EBGM 05	EBGM	EBGM 95
Fexofenadine					
	gastrointestinal tract disorders congenital	10	7.4	13.4	24.6
	cardiac and vascular disorders congenital	20	5.5	8.5	13.1
	cardiac arrhythmias	210	3.0	3.5	4.0
	cardiac and vascular investigations (excl enzyme tests)	86	2.2	2.7	3.3
	hepatic and hepatobiliary disorders	109	2.0	2.4	2.9
Cetirizine					
	neurological disorders congenital	25	8.0	11.9	17.6
	gastrointestinal tract disorders congenital	13	4.2	7.2	12.3
	endocrine disorders congenital	3	4.0	10.8	29.3
	chromosomal abnormalities and abnormal gene carriers	9	3.8	7.2	13.6
	foetal complications	19	3.8	6.0	9.3
	musculoskeletal and connective tissue disorders congenital	22	2.7	4.1	6.2
	immunology and allergy investigations	37	2.4	3.3	4.6
	obstetric and gynaecological therapeutic procedures	29	2.2	3.2	4.6
	immune system disorders congenital	2	2.1	6.6	20.9
	skin vascular abnormalities	56	2.0	2.7	3.5
	chemical injury and poisoning	118	2.0	2.4	2.9
Loratadine					
	reproductive tract and breast disorders congenital	26	25.5	37.5	55.1
	musculoskeletal and connective tissue disorders congenital	22	4.4	6.6	10.1
	cardiac arrhythmias	472	4.2	4.6	5.1
	gastrointestinal tract disorders congenital	9	3.7	7.0	13.1
	renal and urinary tract disorders congenital	7	3.1	6.3	12.8
	cardiac and vascular investigations (excl enzyme tests)	139	2.3	2.7	3.2
	chemical injury and poisoning	87	2.1	2.6	3.2
	hepatic and hepatobiliary disorders	176	2.0	2.3	2.7

We request you assess if there are safety signals, and what is their significance? Of note, we consulted the Division of Cardiorenal Products to review the ECG/QT data from the clinical trials conducted by the Sponsor. Please contact Linda Hu at ext 6-0918 if you have any questions.

SIGNATURE OF REQUESTER Jessica Diaz	METHOD OF DELIVERY (Check one) DARRTS X☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201613	ORIG-1	SANOFI AVENTIS US LLC	Allegra (Fexofenadine Hcl) oral tablets
NDA-201373	ORIG-1	SANOFI AVENTIS US LLC	FEXOFENADINE HCL
NDA-21909	SUPPL-3	SANOFI AVENTIS US LLC	ALLEGRA (FEXOFENADINE HCL)

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/s/

JESSICA M DIAZ
06/21/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021909/S-003
NDA 201373
NDA 201613

INFORMATION REQUEST

sanofi-aventis, U.S., LLC
Attention: Mary-Beth Wigley, B.S., M.S.
Assistant Director, Regulatory R & D Portfolio,
Global Regulatory Affairs
9 Great Valley Parkway
P.O. Box 3026, GV31-123
Malvern, PA 19355

Dear Ms. Wigley:

Please refer to your New Drug Application (NDA) dated March 25, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product	**NDA Number**
ALLEGRA®, (fexofenadine HCl) orally disintegrating tablets, 30mg	021909/S-003
ALLEGRA® (fexofenadine HCl) oral suspension, 30 mg/ 5 mL	201373
ALLEGRA®, (fexofenadine HCl) tablets, 30, 60, and 180 mg	201613

We are reviewing the Clinical section of your submission and have the following comments and information requests. We request a written response in order to continue our evaluation of your NDAs. Please submit the following studies for review:

1. Study PJPR0028: Drug-drug interaction study between fexofenadine and ketoconazole.
2. Study PJPR0018: Drug-drug interaction study between fexofenadine and erythromycin.
3. Study M016455/1105: Drug-drug interaction study between fexofenadine and erythromycin.
4. Study PJPR0043: Drug-drug interaction study between fexofenadine and pseudoephedrine.

If you have any questions, call Jessica M. Diaz, Regulatory Project Manager, at (301) 796-4908.

Sincerely,

{See appended electronic signature page}

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201613	ORIG-1	SANOFI AVENTIS US LLC	Allegra (Fexofenadine Hcl) oral tablets
NDA-201373	ORIG-1	SANOFI AVENTIS US LLC	FEXOFENADINE HCL
NDA-21909	SUPPL-3	SANOFI AVENTIS US LLC	ALLEGRA (FEXOFENADINE HCL)

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/s/

MARY RUSSELL R VIENNA
06/21/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 201373

FILING COMMUNICATION

sanofi-aventis, U.S., LLC
Attention: Mary-Beth Wigley, B.S., M.S.
Assistant Director, Regulatory R & D Portfolio,
Global Regulatory Affairs
9 Great Valley Parkway
P.O. Box 3026, GV31-123
Malvern, PA 19355

Dear Ms. Wigley:

Please refer to your new drug application (NDA) dated March 25, 2010, received March 25, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for ALLEGRA®, (fexofenadine HCl), tablets, 30, 60, and 180 mg.

We also refer to your submissions dated May 6 and May 7, 2010.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is January 25, 2011.

We are reviewing your supplemental application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by December 17, 2010.

During our filing review of your application, we identified the following potential review issues and information requests:

Clinical Pharmacology

1. The application did not contain complete study reports of the 13 studies related to clinical pharmacology in module 5. Submit full study report for studies M016455/J001, M016455/J002, M016455/1122, M016455J/1104, M016455Q/1124, M016455Q/1125, M016455/4124, M016455/1105, M016455I/1120, M016455/4123, M016455/J003, M016455/J006, and M016455I/1119.

Labeling

2. Submit the annotated font specifications for the Drug Facts Label.

Clinical

3. Create a dataset from the DEMOG Dataset with a record for each study and the fields GROUP, STUDYID, TITLE and hyperlink to study synopsis.
4. Provide a narrative discussion and analysis of the literature pertaining to the *Adverse Events of Special Interest* that you have previously identified in your submission (including cardiac and ventricular arrhythmic events, interactions, etc.).
5. For the section *Adverse Events of Special Interest*, provide case numbers and hyperlinks to the serious case reports being referenced.

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

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

If you have any questions, call Jessica Diaz, Regulatory Project Manager, at (301) 796-4908.

Sincerely,

{See appended electronic signature page}

Andrea Leonard-Segal, M.D.
Director
Division of Nonprescription Clinical Evaluation
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201373	ORIG-1	SANOFI AVENTIS US LLC	FEXOFENADINE HCL

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

/s/

ANDREA LEONARD SEGAL
06/07/2010

David, Jeannie C

From: David, Jeannie C
Sent: Monday, May 03, 2010 12:57 PM
To: 'Judy.Plon@sanofi-aventis.com'
Cc: Adams-King, Janice; Mary-Beth.Wigley@sanofi-aventis.com
Subject: RE: Allegra NDAs 201613 and 201373
Importance: High

Hi Judy,

Per our conversation today, we would like to request the following information.

For NDA 201,613, we are reviewing the Establishment information provided in Tables 1 and 2 in Module 1 Section 1.1.2 (Attachment to Form 356h):

1. We would like further information on the Sanofi-aventis Deutcheland GmbH site in Frankfurt am Main, Germany. Helpful information would include: a) a street address if applicable, b) confirmation of the Establishment Registration Number provided, c) date of change of ownership for the site, d) date of last inspection. If there is updated information for items a) or b), please amend Module 1 Section 1.1.2 to include this information.

2. For the (b) (4), please a) confirm the zip code provided, b) clarify the packaging responsibilities (e.g., primary, secondary), as well as if there are any labeling responsibilities at the site, and c) confirm the Establishment Registration Number provided. Please amend Module 1 Section 1.1.2 to include this information.

3. In addition to the five facilities provided in Table 2 of Module 1 Section 1.1.2, we have found the following four facilities listed under 3.2.P.3 Manufacture in Drug Product Cross-Reference Table provided in Module 2 Quality Overall Summary:

(b) (4)

S-009 CBE-30 – addition of Aventis Pharma, Inc., Laval, Quebec as alternate manufacturing, packaging, labeling, testing and release site for the 180 mg tablet product

S-020 CBE-30 – addition of sanofi-aventis site at Fawdon, Newcastle Upon Tyne, United Kingdom, as alternate manufacturing site for 180 mg tablet product; includes contract lab for microbiological testing

Please clarify whether these four facilities will involve in the drug product manufacture for NDA 201613, and amend Module 1 Section 1.1.2 for any missing drug product manufacturing/testing facilities.

For NDA 201,373, we are reviewing the Establishment information provided in Tables 1 and 2 in Module 1 Section 1.1.2 (Attachment to Form 356h):

1. We have the same question as 1. above for NDA 201,613.

2. For the Sanofi-aventis U.S. LLC site in Kansas City, MO, we note in both Table 2 in Module 1, Attachment to Form 356h, and Table 1 in Module 3.2.P.3.1 Manufacturer, that the site(s) Stability Testing operations have not been designated. Please amend Module 1 Section 1.1.2 to include this information.

If you have any questions, please contact me. I look forward to your call later today.

Best regards,

Jeannie

Jeannie David, M.S.
Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of New Drug Quality Assessment
10903 New Hampshire Avenue
Building 22, Mail Room 1491
Silver Spring, MD 20993
Phone: (301) 796-4247
Fax: (301) 796-9877

jeannie.david@fda.hhs.gov

From: Judy.Plon@sanofi-aventis.com [mailto:Judy.Plon@sanofi-aventis.com]
Sent: Tuesday, April 27, 2010 12:05 PM
To: David, Jeannie C
Cc: Adams-King, Janice; Mary-Beth.Wigley@sanofi-aventis.com
Subject: Allegra NDAs 201613 and 201373

Hi Jeannie,

I am Mary-Beth Wigley's supervisor. She is out of the office this week. She forwarded your voice mail to me.

Please forward the CMC questions which you described in your voice mail and I will follow up for you.

Thanks, Judy

Judith Plon
sanofi-aventis U.S. Inc
Regulatory Development
610-889-6947 (office)
215-421-1447 (cell

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201373	ORIG-1	SANOFI AVENTIS US LLC	FEXOFENADINE HCL

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/s/

JEANNIE C DAVID
05/03/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 201613, Allegra® (Fexofenadine HCl) tablets
NDA 201373, Allegra® (Fexofenadine HCl) oral suspension **NDA ACKNOWLEDGMENT**

Sanofi-Aventis, U.S., LLC
Attention: Mary-Beth Wigley, B.S., M.S.
Assistant Director, Regulatory R & D Portfolio,
Global Regulatory Affairs
9 Great Valley Parkway
P.O. Box 3026, GV31-123
Malvern, PA 19355

Dear Ms. Wigley:

We have received your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product	**NDA Number**
Allegra® (fexofenadine HCl 30 mg, 60 mg, 180 mg) tablets	201613
Allegra® (fexofenadine HCl 30 mg/ 5 mL) oral suspension	201373

Date of Application: March 25, 2010

Date of Receipt: March 25, 2010

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on May 24, 2010 in accordance with 21 CFR 314.101(a).

The NDA numbers provided above should be cited at the top of the first page of all submissions to these applications. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

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

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however,

it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm

If you have any questions, call me at (301) 796-3713.

Sincerely,

{See appended electronic signature page}

Janice Adams-King, RN, BSN, MS
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201613	ORIG-1	SANOFI AVENTIS SPA	Allegra (Fexofenadine Hcl) oral tablets
NDA-201373	ORIG-1	SANOFI AVENTIS US INC	FEXOFENADINE HCL

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/s/

JANICE Adams
04/09/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Office/Division)*: DCRP			FROM (*Name, Office/Division, and Phone Number of Requestor)*: Janice Adams-King, ODE IV/DNCE, 6-3713	
DATE 04-02-2010	IND NO.	NDA NO. 201613, 201373 and sNDA 21909	TYPE OF DOCUMENT 2 New NDAs and 1 efficacy supplement	DATE OF DOCUMENT March 26, 2010
NAME OF DRUG Allegra	PRIORITY CONSIDERATION High		CLASSIFICATION OF DRUG antihistamine	DESIRED COMPLETION DATE October 26, 2010

NAME OF FIRM: Sanofi-Aventis

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE / ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END-OF-PHASE 2a MEETING
- ☐ END-OF-PHASE 2 MEETING
- ☐ RESUBMISSION
- ☐ SAFETY / EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

- ☐ PRIORITY P NDA REVIEW
- ☐ END-OF-PHASE 2 MEETING
- ☐ CONTROLLED STUDIES
- ☐ PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):
- ☐ CHEMISTRY REVIEW
- ☐ PHARMACOLOGY
- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE 4 STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL - BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG SAFETY

- ☐ PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ NONCLINICAL

COMMENTS / SPECIAL INSTRUCTIONS:

Sanofi Aventis has submitted applications for the Rx-to-OTC switch of fexofenadine (Allegra) tablets, oral disintegrating tablets, and oral suspension (NDA 201-613, 201-373 and 21-909). We are reexamining the safety profile of fexofenadine as part of the switch applications. The NDA submissions include an analysis of ECGs obtained in clinical studies submitted for previously approved fexofenadine NDAs, in addition to new ECG data not previously submitted to the FDA. The analyses include the evaluation of changes of ECG parameters from baseline and frequencies of potentially clinically significant ECG changes.

We are consulting with you to evaluate the ECG data and cardiac adverse event data (especially post-marketing data--see section 6 in the ISS starting on p.107 and cardiac adverse event information in the Adverse Events of Special Interest section of the Postmarketing Report) for the 2 new NDAs and the 1 efficacy supplement. The safety data analysis, presented in the ISS (section 5.3.5.3) of these three submissions, is identical. Please review and advise if there are cardiac safety concerns with fexofenadine.

Please note the filing date is May 24, 2010.

SIGNATURE OF REQUESTOR Janice Adams-King	METHOD OF DELIVERY (Check one) ☒ DFS ☒ EMAIL ☐ MAIL ☐ HAND
PRINTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201613	ORIG-1	SANOFI AVENTIS SPA	Allegra (Fexofenadine Hcl) oral tablets
NDA-201373	ORIG-1	SANOFI AVENTIS US INC	FEXOFENADINE HCL
NDA-21909	SUPPL-3	SANOFI AVENTIS US LLC	ALLEGRA (FEXOFENADINE HCL)

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/s/

JANICE Adams
04/08/2010

FINANCIAL DISCLOSURE

Sanofi-aventis, U.S. has provided all the financial disclosure information for the covered clinical studies (PJPR0057, M016455M/M3001, M016455M/M3002, and M016455M/M3097) in support of the switch from prescription to non-prescription use of the mono-products of fexofenadine HCl and the fixed-dose combination products of fexofenadine HCl and pseudoephedrine HCl in NDA 201-613, Sequence No. 0000, Section 1.3.4 Financial Disclosure.

FINANCIAL DISCLOSURE

Financial disclosure information is provided for the studies identified below:

M016455I/1003: Two-Way Crossover, Randomized, Open-Label Pivotal Study Comparing the Bioavailability of Fexofenadine Hydrochloride Suspension in Fed and Fasted Healthy Adult Subjects

M016455I/1004: Two-Way Crossover, Randomized, Open-Label Pivotal Bioequivalence Study Comparing the Fexofenadine Hydrochloride Suspension to the Marketed Allegra Tablet in Healthy Adult Subjects

M016455I/1005: A Multicenter Study to Assess the Safety and Pharmacokinetics of Open-Label 30 mg Single Dose Fexofenadine Hydrochloride Oral Suspension (6mg/mL) in Pediatric Subjects 2 to 5 Years of Age

There were no investigators in these studies that replied "yes" to the financial arrangement question on the financial disclosure form (Form FDA 3454) attached.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

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

12/15/05

TO BE COMPLETED BY APPLICANT

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

Please mark the applicable checkbox.

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

(b) (4)

[redacted]

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

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

NAME	TITLE
Douglas Greene, M.D.	US Corperate Regulatory Affairs
FIRM / ORGANIZATION: Aventis Pharmaceuticals, a member of the sanofi-aventis group	
SIGNATURE	DATE: 12/15/05

Paperwork Reduction Act Statement

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

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

Reference ID: 2920249

FORM FDA 3454 (2/03)

Form Approved: OMB No. 0910 - 0297 Expiration Date: January 31, 2010 See Instructions for OMB Statement, below.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

PRESCRIPTION DRUG USER FEE COVERSHEET

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

1. APPLICANT'S NAME AND ADDRESS

SANOFI AVENTIS US LLC
Waynette Shafer
9 GREAT VALLEY PARKWAY
Malvern PA 19355
US

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

201-373

2. TELEPHONE NUMBER
610-889-8972

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?

[X] YES [ ] NO

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

[ ] THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION

[X] THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

201613

3. PRODUCT NAME
ALLEGRA - oral suspension (fexofenadine)

6. USER FEE I.D. NUMBER
PD3010155

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

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

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

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

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

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

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

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

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

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

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Mary Beth Wigley	Assistant Director Global Regulatory Affairs	23 Feb 2010

9. USER FEE PAYMENT AMOUNT FOR THIS APPLICATION
$702,750.00

Form FDA 3397 (03/07)

Close Print Cover sheet

1 Page(s) has been Withheld in Full as B4 (CCI/TS) immediately following this page