

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-375**

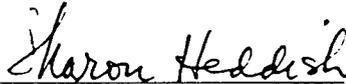
**ADMINISTRATIVE and CORRESPONDENCE  
DOCUMENTS**

**Paragraph III Patent Certification  
Loratadine Orally Disintegrating Tablet 10 mg**

Whitehall-Robins Healthcare hereby certifies that in its opinion and to the best of its knowledge, U.S. Patent No. 4,659,716 will expire on October 21, 2004.

Whitehall-Robins Healthcare hereby certifies that in its opinion and to the best of its knowledge, U.S. Patent No. 4,863,931 will expire on March 15, 2009.

Whitehall-Robins Healthcare hereby certifies that in its opinion and to the best of its knowledge, U.S. Patent No. 4,282,233 will expire on December 19, 2002.



Sharon Heddish

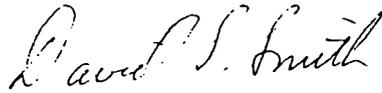
Vice President, Worldwide Regulatory Affairs

Whitehall-Robins Healthcare  
New Drug Application  
August 23, 2001

NDA 21,375  
Loratadine 10 mg Orally Disintegrating Tablet

**ITEM 16: DEBARMENT STATEMENT**

Whitehall-Robins Healthcare hereby certifies that it did not and will not use in any capacity the services of any person debarred under Sections 306 of the Act in connection with such application.



David S. Smith PhD  
Director, Regulatory Affairs

## MEMORANDUM OF TELEPHONE CONFERENCE MINUTES

**MEETING DATE:** December 4, 2002  
**LOCATION:** Zeccola's Office  
**APPLICATION:** NDA 21-375 Alevert

### FDA ATTENDEES, TITLES, AND OFFICE/DIVISION

#### Representatives of FDA

Anthony Zeccola, Regulatory Management Officer

#### Representatives of Wyeth Consumer Healthcare

Sharon Heddish, Vice President, Regulatory Affairs  
Lauren Quinn, Associate Director, Regulatory Affairs  
David Smith, Ph.D., Director, Regulatory Affairs

**Background:** This teleconference was held as follow-up to Wyeth's October 31, 2002 submission in which they responded to our telephone facsimile dated October 29, 2002. While the intention of the 10/29/02 facsimile was primarily to convey CMC comments (the responses to which have been addressed in the most recent CMC review), it also contained the following labeling comments:

2. The following comments pertain to the labeling.
  - a). Increase font size and enhance prominence of the established name "Loratadine Orally Disintegrating Tablet, 10 mg",
  - b). Remove the word "Antihistamine" from the parenthesis. "Antihistamine" is not part of the established name.

In their 10/31/02 response, Wyeth agreed "to revise the labeling accordingly." Subsequent to that date, Wyeth indicated that they had already printed the label as submitted in their October 14, 2002 submission, which they would like to be able to use during their initial distribution of the product.

**Discussion:** During the course of this telephone conversation, the Wyeth representatives committed to implementing the changes listed above, at the time of the second printing of the label. The Tentative Approval, as well as the final Approval letter, will contain a statement reminding them of this commitment.

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/s/

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Anthony Zeccola  
12/12/02 02:24:24 PM  
CSO



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

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE:** November 21, 2002

<b>To:</b> Ms. Lauren Quinn	<b>From:</b> Anthony M. Zeccola
<b>Company:</b> Wyeth Consumer Healthcare	Division of Pulmonary and Allergy Drug Products
<b>Fax number:</b> 973-660-8761	<b>Fax number:</b> 301-827-1271
<b>Phone number:</b>	<b>Phone number:</b> 301-827-1058

**Subject:** Post Marketing Agreement Request – NDA 20-375

**Total no. of pages including cover:** 3 (including electronic signature page)

**Comments:**

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**Document to be mailed:**       YES       NO

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November 1, 2002 Fax

Page 2

The Division of Pulmonary and Allergy Drug Products and the Division of Over-the-Counter Drug Products have identified an issue for your NDA for Alevert (loratadine) that we believe warrants additional follow-up, post approval. In order to complete the action on your NDA, it will be necessary for you to provide a written agreement to address this issues as described below, which will then be referenced in the action letters. If you do not agree, you may call me at (301) 827-1058 or Elaine Abraham at (301) 827-2301, to set up a time to discuss this matter.

**Agreement for loratadine-containing products regarding hypospadias**

**Periodic Safety Update Reports**

You should provide a written agreement to provide an update on the possible association of hypospadias with loratadine use in pregnancy. Spontaneous reports for hypospadias must be summarized in a separate section of the required quarterly periodic safety update reports and annual periodic safety update reports. This section of the annual periodic safety update reports should contain a narrative discussion, analysis, and summary of any and all such events. You should provide an update on data from the Swedish Medical Birth Registry (SMBR). You should also summarize information from other sources, such as the Motherisk database, and regulatory authorities in other countries. Information from the SMBR and other sources should include data listings, summary tables, analysis, and interpretation. Reports should also include information on any regulatory action taken or any changes of the marketing status of the product worldwide as a result of these events. A summary and analysis of the worldwide literature review for loratadine and hypospadias should also accompany each required annual periodic safety report. These reports are required for 3 years.

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/s/

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Anthony Zeccola  
11/21/02 01:12:01 PM  
CSO



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

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE: October 28, 2002**

<b>To:</b> David Smith	<b>From:</b> Sandy Barnes
<b>Company:</b> Whitehall-Robbins Healthcare	Division of Division of Pulmonary and Allergy Drug Products
<b>Fax number:</b> 973-660-8698	<b>Fax number:</b>
<b>Phone number:</b> 973-660-6806	<b>Phone number:</b> (301) 827-1055
<b>Subject:</b> NDA 21-375	

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**Total no. of pages including cover: 2**

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**Comments:**

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**Document to be mailed:**             YES             NO

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1. The following comments pertain to your Response 1.

a). Tighten the proposed color specification for drug product as follows:

\_\_\_\_\_

\_\_\_\_\_

b). Tighten the proposed color specification for drug substance as follows:

\_\_\_\_\_

\_\_\_\_\_

2. The following comments pertain to the labeling.

a). Increase font size and enhance prominence of the established name "Loratadine Orally Disintegrating Tablet, 10 mg".

b). \_\_\_\_\_

3. Provide updated drug substance specifications, drug product release specifications, and stability specifications reflecting the agreed color specifications.

4. Provide 3 copies of updated method validation packages.

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/s/

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Sandra Barnes  
10/28/02 05:21:04 PM  
CSO

**Division of Over-the-Counter Drug Products  
Addendum Labeling Review**

NDA # 21-375

Amendment Date : 10/14/02

Review Date : 10/21/02

Applicant: Wyeth Consumer Healthcare  
Five Giralda Farms  
Madison, NJ 07940

Applicant's  
Representative: David S. Smith  
Director, Regulatory Affairs  
Development & Regulatory Affairs

Drug: Alavert™ Allergy - Loratadine Orally Disintegrating Tablet, 10 mg

Pharmacological Category: Antihistamine

Submitted: *Alavert™ Allergy*  
- 12-, 24- and 48-count carton revised draft label

**Background:**

In response to the approvable letter dated September 19, 2002, for OTC Alavert Allergy drug product (NDA 21-375), the sponsor submitted revised draft labeling for its Alavert Allergy 12-, 24-, and 48-count carton labels on October 14, 2002. The sponsor also indicated in this submission that it agrees to withdraw the alternate Dimetapp brand name at this time.

**Reviewer comments:**

The sponsor incorporated all of the Agency's required and recommended labeling changes for the Alavert Allergy 12-, 24-, and 48-count carton labels. The labeling is acceptable.

The sponsor has decided not to exercise the option of adding the phrase ' ——— ' to the name of the Alavert Allergy product. Therefore, the draft labeling for the 6-count blister card label submitted by the sponsor on July 19, 2002, is also acceptable.

**Recommendations:**

1. A tentative approval letter can be issued to the sponsor requesting final printed 12-, 24-, and 48-count carton and 6-count blister card labels. The final printed carton labels must be identical to the labels submitted on October 14, 2002, and the final printed 6-count blister card label must be identical to the blister card label submitted on July 19, 2002.
2. Inform the sponsor that the word "NEW!" must be deleted from the PDP six months after introduction into the market place.

/s/

\_\_\_\_\_  
Cazemiro R. Martin  
IDS: Reg. Review Scientist

/s/

\_\_\_\_\_  
Concur: Marina Chang, R.Ph.  
Team Leader

6 page(s) of  
revised draft labeling  
has been redacted  
from this portion of  
the review.

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/s/

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Cazemiro Martin  
10/21/02 11:37:55 AM  
INTERDISCIPLINARY

Marina Chang  
10/21/02 02:58:43 PM  
INTERDISCIPLINARY

## MEMORANDUM OF TELECONFERENCE MINUTES

**MEETING DATE:** October 4, 2002  
**TIME:** 1:45 PM  
**LOCATION:** Zeccola's Office  
**APPLICATION:** NDA 21-375 Alevert (loratadine 10mg orally disintegrating tablets)

### **Division of Pulmonary and Allergy Drug Products Participants:**

Chong Ho Kim, Ph.D., Chemist  
Anthony M. Zeccola, Regulatory Management Officer

### **Wyeth Consumer Healthcare Participants:**

Julia Kim Ph.D., Associate Director Regulatory Affairs  
Sharon Heddish, VP Global Regulatory Affairs  
David Smith Ph.D., Director Regulatory Affairs.

**Background:** As follow-up to the September 26, 2002 meeting between representatives of Wyeth and the Agency, Wyeth submitted their proposals for Microbiology Test Specifications and Color Test Methods for Division comment prior to submission of their complete response to the Agency's September 19, 2002, Approvable Letter. This submission, sent via electronic mail, was dated October 4, 2002 (see attachment).

### **Discussion**

1. **Microbial Test Specification** - Based on the information presented in the October 4, 2002 submission, the proposed Microbial Test Specifications appear to be acceptable as tentative specifications. Because one of the batches tested was above the suggested limit of \_\_\_\_\_ the applicant was advised to amend this specification as additional production data become available.
2. **Color Test Specification** – Based on the data available at this time, either of the proposed methods appear to be acceptable. Since only limited data are available at this time, the applicant was advised to propose a specification using either of the methods, based on the current data. This specification will be considered as a tentative specification, and should be revised as addition production data become available.
3. When submitting the complete response to the September 19, 2002 Approvable Letter, the Applicant should include an updated Methods Validation Package.

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/s/

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Anthony Zeccola  
10/7/02 10:08:00 AM  
CSO



DEPARTMENT OF HEALTH & HUMAN SERVICES  
Public Health Service  
Food and Drug Administration  
Center for Drug Evaluation and Research

**MEMORANDUM**

**DATE:** Tuesday, September 17, 2002  
**FROM:** Robert J. Meyer, Director, ODE II  
**TO:** File; NDA 21-375 Alavert (loratadine) Orally Disintegrating Tablets  
**SUBJECT:** NDA action

This is to document with concurrence of the Office of Drug Evaluation II with the reviews, conclusions and action letter for the 2nd cycle review on NDA 21-375. There are remaining CMC and labeling issues that preclude a tentative approval action at this point in time. A full Office memorandum will be written with the approval/tentative approval action if and when this occurs.

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/s/

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Robert Meyer  
9/17/02 09:16:47 AM  
MEDICAL OFFICER

**ADRA Review #1 of Action Package for NDA 21-375, Alavert Orally-Disintegrating Tablets (loratadine, 10 mg).**

Reviewer: Lee Ripper, HFD-102

Date received in HFD-102: July 1, 2002

Date of Review: July 1, 2002

Date original NDA received: September 4, 2001

UF GOAL DATE: July 4, 2002

Indication: Relief of symptoms due to hay fever or other upper respiratory allergies

Action type: AE

RPM: Tony Zeccola, X 7-1058

Drug Classification: 3SN

505(b)(2) application

Patent Info: Paragraph III certification. (Does not require notification of patent holder.)

EA: CE, page 39 of CMC review #1

EER: AC 5/9/02

Clinical Inspection Summary: No clinical inspections

Debarment statement: AC

Safety Update: SU dated 5/23/02 received. See p. 25 of MOR #1 by C. Lee

DMETS Review of Trade Name: Pending.

DOTCDP Review: Pending

1. Financial disclosure information/review: Financial disclosure information is not discussed in either the MOR or the biopharm review. FD submission does not identify the studies for which FD information was submitted.
2. Comments on letter given to RPM.

Pkg n  
JC  
DS' memo

**ADRA Review #2 of Action Package for NDA 21-375, Alavert Orally-Disintegrating Tablets (loratadine, 10 mg).**

Reviewer: Lee Ripper, HFD-102

Date received in HFD-102: September 16, 2002

Date of Review: September 16, 2002

Date original NDA received: September 4, 2001

UF GOAL DATE: September 19, 2002

Indication: Relief of symptoms due to hay fever or other upper respiratory allergies

Action type: AE

RPM: Tony Zeccola, X 7-1058

Drug Classification: 3SN

505(b)(2) application

Patent Info: Paragraph III certification. (Does not require notification of patent holder.)

EA: CE, page 39 of CMC review #1

EER: AC 5/9/02

Clinical Inspection Summary: BE study was audited, found AC for review

Debarment statement: AC

Safety Update: Satisfactory

1. Financial disclosure information/review: Financial disclosure information is not discussed in the MOR, medical TL review, or biopharm review. FD submission does not identify the studies for which FD information was submitted. This point needs to be clarified as FD information is required for the study showing bioequivalence to the reference listed drug.
2. Has the DSI review been put into DFS? There is no DFS signature page with the copy of the review in the action package.
3. 7/19/02 submission needs to be recoded from BZ to AZ.
4. See comments on letter.

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/s/

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Leah Ripper  
9/16/02 07:13:32 PM  
CSO

**Division of Over-the-Counter Drug Products  
Addendum Labeling Review**

NDA # 21-375

Amendment Date : 7/19/02  
Review Date : 8/07/02

Applicant: Wyeth Consumer Healthcare  
Five Giralda Farms  
Madison, NJ 07940

Applicant's Representative: David S. Smith  
Director, Regulatory Affairs  
Development & Regulatory Affairs

Drug:

1. **Alavert™ Allergy**  
Loratadine Orally Disintegrating Tablet, 10 mg
  
2. **Children's Dimetapp® Allergy**  
Loratadine Orally Disintegrating Tablet, 10 mg

Pharmacological Category: Antihistamine

Submitted:

1. **Alavert™ Allergy**
  - 12-, 24- and 48-count carton revised draft label
  - 6-count blister card revised draft label
  
2. **Children's Dimetapp® Allergy:** \_\_\_\_\_

**Background:**

In response to the approvable letter dated July 3, 2002, for OTC Alavert Allergy drug product (NDA 21-375), the sponsor submitted revised draft labeling on July 19, 2002, for its Alavert Allergy 12-, 24-, and 48-count carton labels. The sponsor also submitted draft \_\_\_\_\_ carton label for a second brand name "Children's Dimetapp".

**Reviewer comments:**

The sponsor incorporated most of the Agency's required and recommended labeling changes for the Alavert Allergy product. However, the sponsor expressed concern with the Agency's recommendation to delete the phrase \_\_\_\_\_ wherever it appears in the labeling of the proposed drug product and the phrase \_\_\_\_\_ that appears on the back panel of the proposed carton label. The sponsor noted that the purpose of the phrase ' \_\_\_\_\_ ' is to describe the dosage form in terms understandable to the consumer. The sponsor stated that a consumer who expects a swallow tablet will be dissatisfied with the sudden melting sensation and may believe the product is defective. According to the sponsor, the phrase \_\_\_\_\_ will avoid such consumer confusion. However, to accurately

represent the — disintegration of the tablet itself, rather than any perceived claims of dissolution, the sponsor proposed an alternative phrase \_\_\_\_\_ instead of the phrase \_\_\_\_\_. To further describe to the consumer what \_\_\_\_\_ means, the sponsor proposed to add the phrase “Melts in the mouth” above the red-ribbon statement “\_\_\_\_\_” on the PDP. The sponsor also listed in order of preference several alternative phrases to \_\_\_\_\_ several of which have cleared trademark review.

This reviewer believes that that the trademark phrase \_\_\_\_\_ is intended to specifically correspond to the proprietary name “Alavert Allergy” and to the orally disintegrating tablet dosage formulation. As such, the phrase \_\_\_\_\_ is considered an extension to the proprietary name “Alavert Allergy”.

Accordingly, this reviewer has no objection to the trademark phrase \_\_\_\_\_ when used as part of the proprietary name of this product (i.e., “Alavert Allergy \_\_\_\_\_”) to specifically designate an orally disintegrating tablet dosage formulation.

The sponsor also disagreed with the Agency’s comment that it is misleading to consumers to represent the tradename “Children’s Dimetapp” as a dose indicated only for the 6-12 year age group, when, in fact, it is the dose suitable for adults as well. The sponsor pointed out that Loratadine is a unique product in that the same dose is appropriate for children as well as adults. According to the sponsor, the fundamental concern about the safety of marketing the same dose form to adults and children is alleviated by the fact that it is the same dose for both groups and therefore, poses no adverse consequence if children were to use the “adult” product.

With regard to the association of the brand name “Dimetapp” with a single ingredient brompheniramine, the sponsor pointed out that although historically such an association existed, the present-day product line is now associated with a number of active ingredients and a number of combinations of active ingredients. According to the sponsor, the issue of having different active ingredients associated with a single brand name is not unique to Dimetapp. The sponsor also stated that the PDP of the proposed Children’s Dimetapp product provides the consumer with the essential information to make an informed purchase, presented in a clear and understandable format. Further, the design of the carton is not similar to any other product in the Dimetapp line.

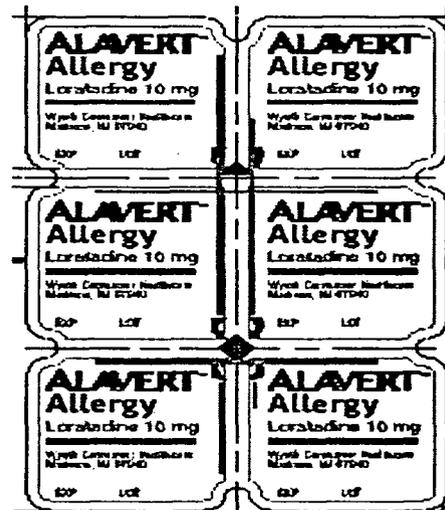
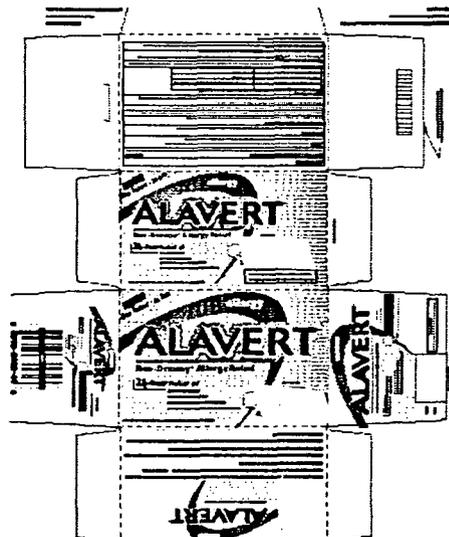
The sponsor noted that trademarks are commercial speech and that FDA may not prohibit the use of an extended brand name unless it is inherently misleading and no other measure (such as clarification in the labeling) will eliminate consumer confusion. According to the sponsor, because the labeling aids the consumer in choosing the appropriate Dimetapp product to prevent confusion, and there is no demonstrated safety issue with the use of the proposed brand name, “Children’s Dimetapp Allergy” is an acceptable name for this product.

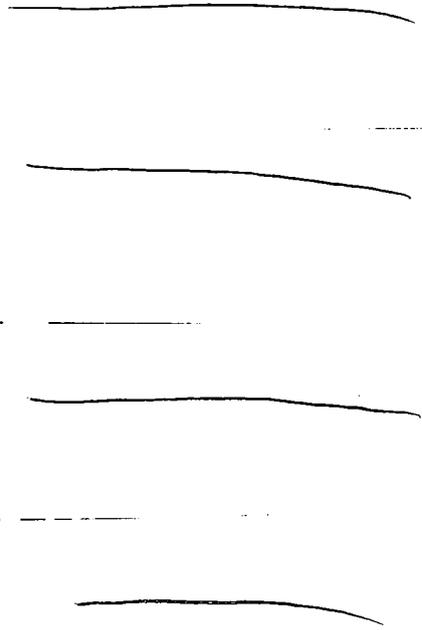
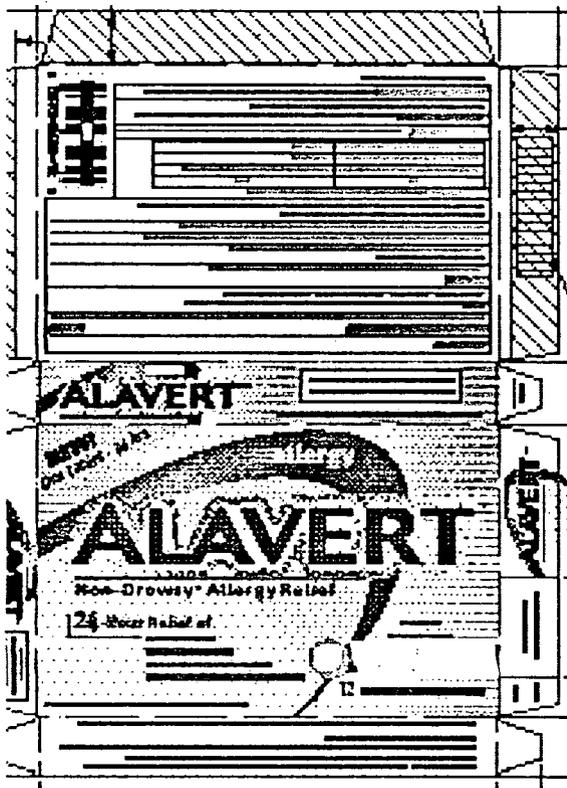
The reviewer has reviewed the sponsor’s response concerning the tradename “Children’s Dimetapp Allergy” and has concluded that this additional tradename is not acceptable. This reviewer has the following comments.

The use “children’s” in the name of the product suggests that this product is specific for use in children. As the sponsor stated, products that include “children’s” in the name offer a formulation that is more acceptable to children to encourage better compliance or ease of administration (e.g., liquid formulation, chewable tablets). In this case, there is no difference in the formulation or dosage regimen from Alavert

Allergy (loratadine orally disintegrating tablets) which is also intended for use by adults and children 6 years and over. This reviewer also notes that the use of “children’s” in the name of a product which is also available in the same dosage form and same dosage regimen for adults, could lead to a proliferation of other products with names based on the age of the population (e.g., “Adolescent [brand name]”, “Elderly [brand name]”). In addition, consumers may purchase these two products, Alavert Allergy and Children Dimetapp Allergy, based on the mistaken belief that each product is specifically intended for adults and children, respectively. This reviewer maintains that consumers are faced with a growing number of product choices for purchase decisions and often find it difficult to determine the product that is best for their particular condition. Because these two products, Alavert Allergy and Children’s Dimetapp Allergy, provide the same dosage form and dosage regimen for both adults and children, this reviewer believes that marketing the product as a children’s product may lead to consumer confusion and consequent suboptimal purchase. Accordingly, the use of “children’s” in the name “Children’s Dimetapp Allergy” is not acceptable.

With regard to the name “Dimetapp”, this reviewer points out that although the popular “Dimetapp” name is now associated with products that offer relief for a wide range of symptoms, consumers may not be able to distinguish a “Dimetapp” product that contains a first generation antihistamine product that causes drowsiness (e.g., brompheniramine) from a second generation “Dimetapp” product that contains a “non-drowsy” antihistamine ingredient (e.g., loratadine). This reviewer believes that it is essential that consumers are fully aware of the distinction between a product that causes drowsiness and a product that does not, particularly with regard to activities that require full attention (e.g., driving or operating machinery). To avoid possible consumer confusion, this reviewer does not believe that it is in the best interest of consumers to have the same brand name “Dimetapp” for a sedating and a non-sedating antihistamine drug product.





1. **CARTON LABELING:** The sponsor submitted revised draft labeling as follows:

*[Reviewer comment: The trade name of this product "Alavert Allergy" is not acceptable. The sponsor should revise the name of this product wherever it appears on the 12-, 24-, and 48-count carton labels to read: "Alavert Allergy". In addition, the red ribbon text " " is not acceptable. The sponsor should delete this red ribbon phrase wherever it appears on the 12-, 24-, and 48-count carton labels. See this reviewer's introductory comments above concerning these labeling issues.]*

**A. PDP:**

- (i) Added the phrase "One Tablet – 24 hrs" immediately after the PDP flag "New".
- (ii) Proposed the asterisk text to read: "\*\*When taken as directed. See Drug Facts panel".
- (iii) Added the phrase "MELTS IN YOUR MOUTH" before red ribbon.

**B. Top Panel and Left Flap: (48-count package only)**

Added the phrase "MELTS IN YOUR MOUTH" before red ribbon.

*[Reviewer comment: The above-mentioned revisions are acceptable.]*

**C. Back Panel:**

- (i) Added the phrase "...when taken as directed", but does not appear in bold type.  
*[Reviewer comment: This phrase should appear in bold type to highlight the manner of use that will generally avoid drowsiness.]*
- (ii) Revised the sentence "The mint flavor...." to read: "The mint flavored \_\_\_\_\_ melts in your mouth".  
*[Reviewer comment: The sponsor must revise the sentence to include the \_\_\_\_\_ of this product, i.e., "The mint flavored \_\_\_\_\_ melts in your mouth".]*

**D. Drug Facts:**

- (i) Revised the first bulleted statement under the Directions section to read: "Tablet melts in mouth. Can be taken with or without water."  
*[Reviewer comment: The revised bulleted text is acceptable.]*
- (ii) Used uppercase letters for certain words in the Directions section (e.g., the first letter of each population group).  
*[Reviewer comment: The following revisions under the Directions section are recommended:*
  - a. *In the first bulleted statement, the first letter in the word "Tablet" should appear in lowercase.*
  - b. *In the dosing table:*
    - 1. *In the first population group, the first letter in the word "Adult" should appear in lowercase.*
    - 2. *In the second population group, the first letter in the words "Children" and "Ask" should appear in lowercase.*
    - 3. *In the third population group, the first letter in the words "Consumers" and "Ask" should appear in lowercase.]*

**2. BLISTER CARD LABEL (Alavert Allergy):**

*[Reviewer comment: The trade name of this product "Alavert Allergy" is not acceptable. The sponsor should revise the name of this product to read: "Alavert Allergy \_\_\_\_\_". See this reviewer's introductory comment above concerning the trade name labeling issue.]*

**3. ANNOTATED LABELING SPECIFICATIONS:**

*[Reviewer comment: The annotated specifications for the Drug Facts graphical features are acceptable.]*

**Recommendations:**

i. The sponsor's 12-, 24-, and 48-count draft carton labels for its Alavert Allergy product are not acceptable. Inform the sponsor that the labeling for these packages need further revision as follows:

A. Trade name and red ribbon phrase \_\_\_\_\_ The trademark phrase \_\_\_\_\_ must not appear in the ribbon sections of the Alavert Allergy 12-, 24- and 48-count draft carton labels. Instead, the sponsor may include this phrase as part of the proprietary name of this product (i.e., "Alavert Allergy \_\_\_\_\_) to specifically designate an orally disintegrating tablet dosage formulation.

The Agency believes that that the trademark phrase \_\_\_\_\_ is intended to specifically correspond to the proprietary name "Alavert Allergy" and to the orally disintegrating tablet dosage formulation. As such, the phrase \_\_\_\_\_ is considered an extension to the proprietary name "Alavert Allergy".

Accordingly, the Agency has not objection to the trademark phrase \_\_\_\_\_ when used as part of the proprietary name (i.e., "Alavert Allergy \_\_\_\_\_) to specifically designate an orally disintegrating tablet dosage formulation. This revised trade name must appear wherever the trade name appears on the **carton and blister card** labels.

B. On the bottom panel of the carton labels:

- (i) The phrase "...when taken as directed" must appear in bold type to highlight the manner of use that will generally result in non-drowsiness.
- (ii) Revise the sentence "The mint flavored \_\_\_\_\_ melts in your mouth" to read: "The mint flavored \_\_\_\_\_ melts in your mouth". See previous discussion in 1(A) above.

2. The Agency recommends the following revisions to the 12- 24-, and 48-count Alavert Allergy draft carton labels:

A. Under the heading Directions:

- (i) In the first bulleted statement, the first letter in the word "Tablet" should appear in lowercase.
- (ii) In the dosing table:
  - a. In the first population group, the first letter in the word "Adult" should appear in lowercase.
  - b. In the second population group, the first letter in the words "Children" and "Ask" should appear in lowercase.
  - c. In the third population group, the letter in the words "Consumers" and "Ask" should appear in lowercase.

B. Under the heading "Questions or comments", the first letter in the word "Call" should appear in lowercase.

3. Inform the sponsor that the brand name "Children's Dimetapp Allergy" is not acceptable. The Agency points out that because there is no difference in the formulation or dosage regimen of the Alavert Allergy and Children's Dimetapp Allergy products, a "children's brand name could lead to a proliferation of other products with names based on specific age groups within the intended

population range. The Agency believes that marketing the product as a children's product may lead to consumer confusion and consequent suboptimal purchase.

In addition, the Agency notes that although the popular "Dimetapp" name is now associated with products that offer relief for a wide range of symptoms, consumers may not be able to distinguish a "Dimetapp" product that contains a first generation antihistamine product that causes drowsiness (e.g., brompheniramine) from a second generation "Dimetapp" product that contains a non-drowsy antihistamine ingredient (e.g., loratadine). The Agency believes that it is essential that consumers be fully aware of the distinction between a product that causes drowsiness and a product that does not, particularly with regard to activities that require full attention (e.g., driving or operating machinery). To avoid possible consumer confusion, the Agency does not believe that it is in the best interest of consumers to have the same brand name "Dimetapp" for a sedating and a non-sedating antihistamine drug product.

5. **For the review chemist:** In the "How Supplied" section of the prescription labeling of Claritin Reditabs (Schering Corporation), the statement "keep in a dry place" appears as a condition of storage. The review chemist should provide the sponsor with appropriate recommendation on this issue in the action letter.

---

Cazemiro R. Martin  
IDS: Reg. Review Scientist

---

Concur: Marina Chang, R.Ph.  
Team Leader

5 page(s) of  
revised draft labeling  
has been redacted  
from this portion of  
the review.

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/s/

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Cazemiro Martin  
8/27/02 09:49:42 AM  
INTERDISCIPLINARY

Marina Chang  
8/27/02 10:47:38 AM  
INTERDISCIPLINARY

## MEMORANDUM OF TELECONFERENCE

**DATE:** June 27, 2002  
**TIME:** 10:30 AM  
**APPLICATION:** NDA 21-375 Loratadine 10mg Orally Disintegrating Tablet  
**APPLICANT:** Whitehall-Robins

**DRAFT**

**Representative of Division of Pulmonary and Allergy Drug Products (DPADP):**  
Anthony M. Zeccola, Regulatory Management Officer (DPADP)

**Representatives of Whitehall-Robins:**  
Lauren Quinn, Associate Directory, Regulatory Affairs  
David Smith, Ph.D., Director, Regulatory Affairs  
Kenneth Warner, Director, CMC Regulatory Affairs

### **Discussion**

The purpose of this telephone conversation was to discuss the final stage of the review of NDA 21-375. As of this date and time, there are still several unresolved issues relating to this application, including unresolved labeling issues and CMC issues (conveyed to the Applicant via telefacsimile on June 11, 2002). The Applicant has been engaged in ongoing labeling negotiations with the Division of Over the Counter Drug Products and has responded to the June 11, 2002, DPADP facsimile via electronic transmissions dated June 14 and June 19, 2002. Following internal discussions with the OTC Division relating to the labeling negotiations and internal CMC discussions (which included review of the June 14<sup>th</sup> and 19<sup>th</sup> communications), it was decided that given the nature and scope of these issues, they could not be resolved prior to the User Fee Goal Date, therefor the Center will issue an Approvable (AE) letter. Whitehall-Robins was encouraged to request a face-to-face meeting prior to responding to the action letter.

The Applicant agreed that this would be an acceptable way to proceed and wanted to discuss the logistics of scheduling the meeting to discuss these issues. The AE letter will contain a complete list of issues which need to be addressed, they should submit a formal meeting request and submit a background document (no later than 30 days prior to the meeting), containing information that they feel will aide in the discussion.

## RECORD OF TELEPHONE CONVERSATION

**Date:** June 21, 2002  
**Project Manager:** Elaine Abraham  
**Subject:** Discuss fax of labeling comments sent June 20, 2000  
**NDA:** 21-375  
**Sponsor:** Wyeth Consumer Healthcare  
**Product Name:** Alavert Allergy/Dimetapp Allergy

**FDA participants:** Elaine Abraham, R.Ph., Project Manager  
Marina Chang, R.Ph., Team Leader  
Rosemarie Neuner, M.D., Medical Officer

**Wyeth participants:** Lauren Quinn, Regulatory Affairs  
David Smith, Regulatory Affairs  
Dr. Wason, Medical Officer

Background: FDA faxed labeling comments to the sponsor on June 20, 2002. The sponsor requested this phone conversation prior to sending in their labeling revisions.

Discussion: The discussion followed the points outlined in the June 20 fax. Any recommendations provided were the reviewer's suggestions. The sponsor is under no obligation to follow the exact wordings.

1. Wyeth will get back to FDA on our recommendation that they withdraw the labeling for the proposed "Children's Dimetapp" product.
2. PDP: (Fax 2a) Wyeth agreed to include the asterisk ("\*") after the phrase "Non-drowsy". However, they plan to propose alternate wording for the footnote, such as

\_\_\_\_\_

The sponsor took issue with the request to delete the phrase \_\_\_\_\_ FDA maintained that the claim is not accurate because in the biostudy, the mean value at the time of peak concentration for the product was 1.04 hours. According to the sponsor, \_\_\_\_\_ is intended to inform the consumer to let the product "melt in the mouth" rather than swallowing. FDA does not believe the term \_\_\_\_\_ 'adequately explains this point and does not consider the term user friendly. In addition, the agency recommended that this information be added to the directions. Also, more data are needed on \_\_\_\_\_. Wyeth contended that \_\_\_\_\_ of the drug dissolves in vitro in \_\_\_\_\_ minutes. However, they will come back with other proposals. Wyeth agreed to the other PDP issues raised in the fax (2b, c, d).

3. Top Panel: Wyeth agreed to the asterisk and will provide further response on the \_\_\_\_\_ issue (see 2. above).

4. Left Flap: Wyeth agreed to the asterisk and will provide further response on the \_\_\_\_\_ issue (see 2. above).
5. Right Flap: Wyeth agreed to the asterisk (see 2. above).
6. Back Panel: Wyeth will propose alternate language to "The mint flavored \_\_\_\_\_ tablet melts in your mouth \_\_\_\_\_" FDA would like data to support this claim. Wyeth agreed to the other Back panel issues raised in the fax (6a, b, c).
7. Drug Facts: [Fax 7h(ii)] Under directions, FDA recommended deleting the bulleted statement \_\_\_\_\_ Wyeth will propose alternate wording, such as, \_\_\_\_\_ Wyeth agrees to the other Drug Facts issues raised in the fax [7a – g, h(i), h(iii), and i].
- 8.-11. Wyeth agrees to FDA's recommendations.

/s/

\_\_\_\_\_  
Elaine Abraham, R.Ph.  
Minutes Preparer

/s/

\_\_\_\_\_  
Marina Chang, R.Ph.  
Concurrence

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/s/

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Elaine Abraham  
7/1/02 01:20:20 PM  
CSO

Marina Chang  
7/1/02 04:29:36 PM  
INTERDISCIPLINARY



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

**FACSIMILE TRANSMITTAL SHEET**

**DATE: June 20, 2002**

<b>To:</b> David S. Smith, Ph.D.	<b>From:</b> Elaine Abraham
<b>Company:</b> Wyeth Consumer Healthcare	Division of Over-the-Counter Drug Products
<b>Fax number:</b> (973) 660-8698	<b>Fax number:</b> (301) 827-2315
<b>Phone number:</b> (973) 660-6806	<b>Phone number:</b> (301) 827-2293
<b>Subject:</b> N 21-375 Labeling review	

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

**Comments:**

**Document to be mailed:**       YES       NO

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**Message:** Please refer to your new drug application NDA 21-375 dated August 23, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Alavert Allergy/Dimetapp Allergy (loratadine 10 mg orally disintegrating tablets).

We have attached reviewer's comments related to the labeling submitted. In order to ensure a timely action for this new drug application, we request that you respond to the issues listed below as soon as possible. You can fax your response to Elaine Abraham at (301) 827-2315.

## Reviewer's Recommendations:

1. Based on the 5/13/02 telephone conversation between Wyeth and the OTC Division, recommendations on the Children's Dimetapp product are not included in this review. The Agency strongly recommends the withdrawal of the labeling for the proposed "Children's Dimetapp" product.

Revise the carton labels of the Alavert™ Allergy product as follows:

### 2. PDP:

- a. Add an asterisk notation ("\*") after the phrase "Non-drowsy". At the bottom of the PDP, the following statement should conspicuously appear as follows: \_\_\_\_\_  
\_\_\_\_\_ See Drug Facts panel." This notation and subsequent statement clarifies when \_\_\_\_\_ may occur.
- b. Revise the established name to read "Loratadine Orally Disintegrating Tablet, 10 mg" to include the dosage form as part of the established name.
- c. Relocate the established name (i.e., revised established name as noted above) and the pharmacological category of the Alavert™ Allergy drug product to appear immediately after the name of the product as described in 21 CFR 201.61. The Agency recommends that the sponsor increase the prominence of this information.
- d. Replace the phrase "12 \_\_\_\_\_ Disintegrating Tablets" with the phrase "12 Orally Disintegrating Tablets", as the name currently recognized by the Agency for this dosage form.
- e. Delete the phrase \_\_\_\_\_ and the associated artwork. The Agency does not consider this statement acceptable based on insufficient data to support this claim.

### 3. Top Panel:

- a. Add an asterisk notation ("\*") after the phrase "Non-drowsy". At the bottom of this top panel, the following statement should conspicuously appear as follows: \_\_\_\_\_  
\_\_\_\_\_ See Drug Facts panel." This notation and subsequent statement clarifies when \_\_\_\_\_ may occur.
- b. Replace the phrase \_\_\_\_\_ with the phrase "Orally Disintegrating". This is the name currently recognized by the Agency for this dosage form.

### 4. Left Flap:

- a. Add an asterisk notation ("\*") after the phrase "Non-drowsy" to direct the consumer to the asterisk statement on the PDP.
- b. Replace the phrase \_\_\_\_\_ with the phrase "Orally Disintegrating". This is the name currently recognized by the Agency for this dosage form.

5. Right Flap: Add an asterisk notation ("\*") after the phrase "Non-drowsy" to direct the consumer to the asterisk statement on the PDP.

6. Back panel (upper-half):

- a. Revise the first sentence to read as follows: "Alavert Allergy provides 24 hours of allergy symptom relief **without causing drowsiness when taken as directed.**" The Agency considers this revision necessary to provide more detailed information to the consumer.
- b. After the first sentence on this panel, add the following parenthetical sentence: "(See Drug Facts below.)". This parenthetical statement is necessary to direct the consumer to the Drug Facts section for more information concerning the non-drowsiness claim.
- c. To avoid consumer confusion, revise the second sentence to read: "It contains prescription strength loratadine."
- d. Delete the sentence  
~~\_\_\_\_\_~~ The Agency believes that this statement implies that  
~~\_\_\_\_\_~~ disintegration results in more ~~\_\_\_\_\_~~ absorption and more ~~\_\_\_\_\_~~ onset of action.  
Further, the Agency points out that this statement is not accurate because the mean value of the time at the peak concentration following the loratadine orally disintegrating tablet was 1.04 hours and 1.21 hours in BE and Food effect study, respectively. This implied claim should be deleted.

7. "Drug Facts" panel:

- a. Under the heading "Active ingredient (in each tablet)", only a single space and no comma should appear between the word "Loratadine" and the strength "10 mg".
- b. Under the heading "Purpose", delete the phrase ~~\_\_\_\_\_~~ "The pharmacological category is "Antihistamine."
- c. Under the heading "Uses", delete the bullet before the word "temporarily."
- d. Add the subheading "Do not use" followed by the text "if you have ever had an allergic reaction to this product or any of its ingredients". The sponsor's reference to ~~\_\_\_\_\_~~ "to this medication or its ingredients" under the subheading "Ask a doctor before use if you have" is misplaced and should be rephrased as noted above.
- e. Immediately after the bulleted statement appearing under the subheading "Ask a doctor before use if you have", add the following statement: "Your doctor should determine if you need a different dose."
- f. Under the subheading "When using this product", the bulleted statement "do not use more than directed" should not be bolded.
- g. Insert the subheading "Stop use and ask a doctor if" followed by the text "an allergic reaction to this product occurs. Seek medical help right away." These statements are consistent with the information appearing under the previous subheading "Do not use."

h. Under the heading "Directions":

- (i) rearrange the bulleted statements for clarity.
- (ii) delete the bulleted statement \_\_\_\_\_ Promotional statements should not appear in the Drug Facts box.
- (iii) add a third population group and text in the dosing table to read as follows: "consumers who have liver or kidney disease: ask a doctor". The Agency considers this dosing information necessary to advise consumers with liver or kidney disease (i.e., conditions that impair drug clearance) to consult with a doctor.

i. Provision for lot number and expiration date must be included.

- 8. Revise the blister card label for the Alavert™ Allergy product by replacing the phrase \_\_\_\_\_ with the phrase "1 Orally Disintegrating Tablet". The net content and the currently recognized name by the Agency for this dosage form must appear on this blister card label.
- 9. \_\_\_\_\_
- 10. Where appropriate on the carton and blister card labels, replace the previous name of the company "Whitehall-Robins Healthcare" with the new company name "Wyeth Consumer Healthcare."
- 11. We reserve comment at this time on the proposed trade name "Alavert Allergy" until the Office of Post Marketing Drug Risk Assessment has commented on this proposed name.

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/s/

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Elaine Abraham  
6/21/02 07:48:19.AM  
CSO

## NDA Labeling Review

NDA # 21-375

Submission Date : 8/23/01  
Amendment Date : 5/24/02  
Review Date : 6/19/02

Applicant: Wyeth Consumer Healthcare  
Five Giralda Farms  
Madison, NJ 07940

Applicant's Representative: David S. Smith  
Director, Regulatory Affairs  
Development & Regulatory Affairs

Drug:

1. **Alavert™ Allergy**  
Loratadine Orally Disintegrating Table, 10 mg
2. **Dimetapp® Allergy 24-Hour** (submitted 8/23/01)  
(Children's Dimetapp®; amendment of 5/24/02)  
Loratadine Orally Disintegrating Tablet, 10 mg

Pharmacological Category: Antihistamine

Submitted:

A. *Alavert™ Allergy*  
- 12-count carton labeling

B. *Dimetapp® Allergy 24-Hour* (submitted 8/23/01)  
*(Children's Dimetapp®)*(Amend. submitted 5/24/01)

### Reviewer Comment:

Loratadine was approved for use in the United States on April 12, 1993 as Claritin (loratadine 10 mg tablets; NDA 19-658). Subsequent approvals for loratadine are as follows:

- Claritin Syrup (loratadine 1.0 mg/mL; NDA 20-641)
- Claritin Reditabs (loratadine 10 mg/mL; oral disintegrating tablets; NDA 20-704)
- Claritin D Extended Release Tablets (loratadine 5 mg/pseudoephedrine sulfate 120 mg; NDA 19-670)
- Claritin-D 24-Hour Extended Release Tablets (loratadine 10 mg/pseudoephedrine sulfate 120 mg; NDA 20-470)

The Schering Corporation produces the Claritin line of products.

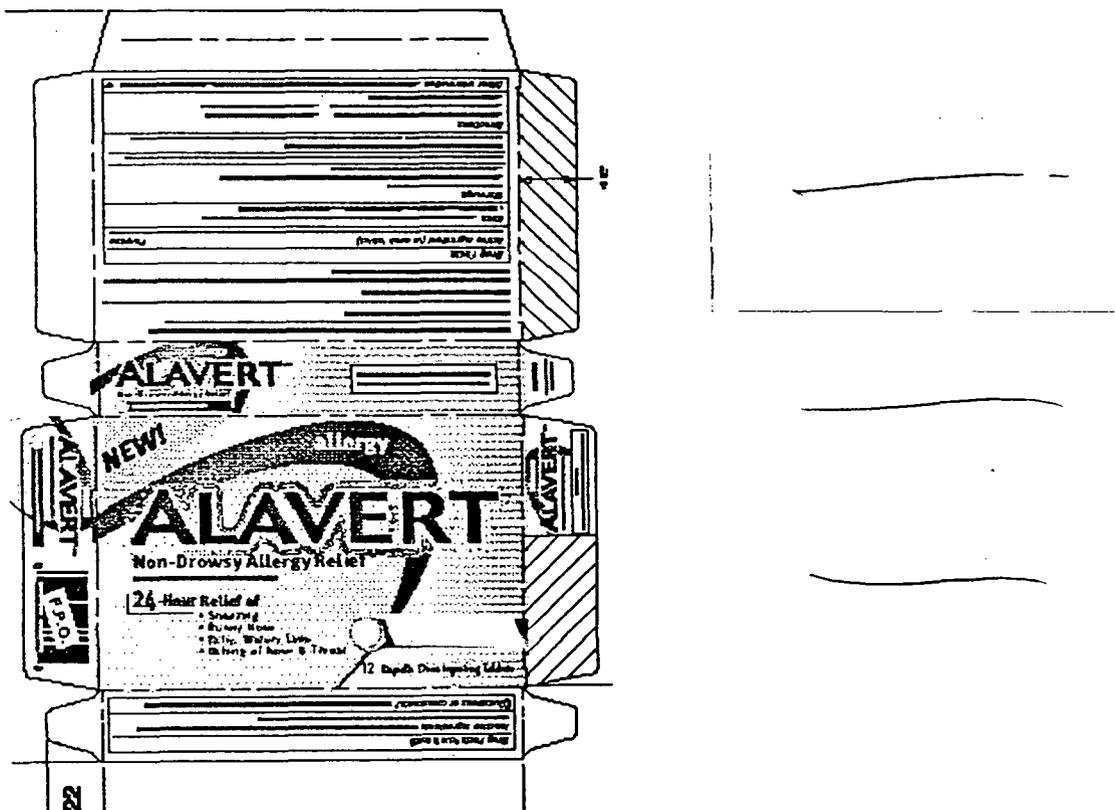
Wyeth Consumer Healthcare is now seeking approval under a 505(b)(2) application (NDA 21-375) to market over-the-counter loratadine 10-mg orally disintegrating tablets. The sponsor intends to market this product under two tradenames: "Alavert™ Allergy", and "Children's Dimetapp®". In the past, FDA has accepted multi-tradenames for the same product.

The annotated specifications submitted by the sponsor for the "Drug Facts" graphical features for the Alavert™ Allergy drug product is satisfactory.

During a telephone conference call on 5/31/02 between the Agency and the sponsor, the Agency noted that several of the company's products have the name "Dimetapp" which are formulated with ingredients, which are different than loratadine. The proposed Children's Dimetapp contains the same formulation and dosage strength as described for the proposed Alavert Allergy product. In addition, the Agency

pointed out to the sponsor that it has only submitted the PDP labeling and not the complete labeling of this product for review and comment. Consequently, the Agency is not aware of the age range that will be proposed in the Directions section of the labeling.

The Agency noted during the telephone conference call, that the sponsor has changed the phrase \_\_\_\_\_ statement to read \_\_\_\_\_ This new way of taking the product may require further chemistry and biopharmaceutics reviews. Based on the above-mentioned review issues, the Agency suggested that the sponsor withdraw the labeling for the Children's Dimetapp product.



Reviewer recommended additions are identified by "redlining" (shaded text) and deletions are identified by "strike out."

A. 12-Count carton labeling (Alavert™ Allergy)

5 page(s) of  
revised draft labeling  
has been redacted  
from this portion of  
the review.

1. Based on the telephone conversation with the sponsor on 5/13/02, review and comment on the Children's Dimetapp product is not included in this review. The Agency strongly recommends that the sponsor withdraw its labeling for the proposed "Children's Dimetapp" product.

2. Inform the sponsor to revise the carton labels of the Alavert™ Allergy product as follows:

A. PDP:

(i) Add an asterisk notation ("\*") after the phrase "Non-drowsy". At the bottom of the PDP, the following statement should conspicuously appear as follows:

See Drug Fact panel." This notation and subsequent statement clarifies when \_\_\_\_\_ may occur.

(ii) Revise the establish name to read "Loratadine Orally Disintegrating Tablet, 10 mg" to include the dosage form as part of the established name.

(iii)

(iv) Replace the phrase "12 \_\_\_\_\_ Disintegrating Tablets" with the phrase "12 Orally Disintegrating Tablets", as the name currently recognized by the Agency for this dosage form.

(v) Delete the phrase ' \_\_\_\_\_ ' and the associated artwork. The Agency does not consider this statement acceptable based on insufficient data to support this claim.

B. Top Panel:

(i) "Add an asterisk notation ("\*") after the phrase "Non-drowsy". At the bottom of this top panel, the following statement should conspicuously appear as follows:

See Drug Fact panel." This notation and subsequent statement clarifies when \_\_\_\_\_ may occur.

(ii) Replace the phrase ' \_\_\_\_\_ ' with the phrase "Orally Disintegrating". This is the name currently recognized by the Agency for this dosage form.

C. Left Flap:

(i) "Add an asterisk notation ("\*") after the phrase "Non-drowsy" to direct the consumer to the asterisk statement on the PDP.

(ii) Replace the phrase \_\_\_\_\_ with the phrase "Orally Disintegrating". This is the name currently recognized by the Agency for this dosage form.

D. Right Flap: Add an asterisk notation ("\*") after the phrase "Non-drowsy" to direct the consumer to the asterisk statement on the PDP.

E. Back panel (upper-half):

(i) Revise the first sentence to read as follows: "Alavert Allergy provides 24 hours of allergy symptom relief **without causing drowsiness when taken as directed.**" The Agency considers this revision necessary to provide more detailed information to the consumer.

(ii) After the first sentence on this panel, add the following parenthetical sentence: "(See Drug Facts below.)". This parenthetical statement is necessary to direct the consumer to the Drug Facts section for more information concerning the non-drowsiness claim.



**A. Prototype: Alavert Allergy - Proposed Drug Facts Labeling<sup>±</sup>**

<b>Drug Facts</b>	
<b>Active ingredient (in each tablet)</b> Loratadine 10 mg.....	<b>Purpose</b> Antihistamine
<b>Uses</b> temporarily relieves these symptoms due to hay fever or other upper respiratory allergies: <ul style="list-style-type: none"> <li>■ runny nose</li> <li>■ sneezing</li> <li>■ itchy, watery eyes</li> <li>■ itching of the nose or throat</li> </ul>	
<b>Warnings</b> Do not use if you have ever had an allergic reaction to this product or any of its ingredients	
Ask a doctor before use if you have <ul style="list-style-type: none"> <li>■ liver or kidney diseases. Your doctor should determine if you need a different dose.</li> </ul>	
When using this product ■ do not take more than directed. Taking more than directed may cause drowsiness.	
Stop use and ask a doctor if an allergic reaction to this product occurs. Seek medical help right away.	
If pregnant or breast-feeding, ask a health professional before use. Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.	
<b>Directions</b> ■ can be taken with or without water	
Adults and children 6 years and over	1 tablet daily; do not use more than 1 tablet in any 24-hour period
children under 6 years	ask a doctor
consumers who have liver or kidney disease	ask a doctor
<b>Other information</b> <ul style="list-style-type: none"> <li>■ Phenylketoneurics: Contains Phenylalanine 8.4 mg per tablet</li> <li>■ store at 20-25°C (68-77°F)</li> </ul>	
<b>Inactive ingredients</b> artificial & natural flavor, aspartame, citric acid, colloidal silicon dioxide, crospovidone, magnesium stearate, mannitol, microcrystalline cellulose, sodium bicarbonate	
<b>Questions or comments?</b> call weekdays from 9 AM to 5 PM EST at 1-800-ROBINS5 (1-800-762-4675)	

<sup>±</sup> The sponsor should follow this Drug Facts label in content only. The font sizes for title, headings, subheadings, condensed text, and other graphic features must be in accordance as set forth in 21 CFR 201.66.

[Lot number and Expiration Date]

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/s/

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Cazemiro Martin  
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Marina Chang  
6/20/02 10:49:16 AM  
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6 page(s) of  
revised draft labeling  
has been redacted  
from this portion of  
the review.



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

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE:** June 11, 2002

<b>To:</b> Ms. Sharon Heddish	<b>From:</b> Ladan Jafari
<b>Company:</b> Whitehall Robins Healthcare	Division of Pulmonary and Allergy Drug Products
<b>Fax number:</b> 973-660-7187	<b>Fax number:</b> 301-827-1271
<b>Phone number:</b> 973-660-5753	<b>Phone number:</b> 301-827-1084
<b>Subject:</b> NDA 21-375	

**Total no. of pages including cover:** 3

**Comments:**

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3. The following comments pertain to the stability of the product.
  - a. Monitor \_\_\_\_\_ as a parameter for the testing of the commercial batches.
  - b. Perform microbial limits tests annually and at expiration.
  - c. The post approval stability protocol and stability commitment presented on pages 171-175, vol. 1 (revision dated December 7, 2000, \_\_\_\_\_) is outdated. Provide an updated version of the post approval stability protocol and stability commitment.
  - d. Tighten the impurities specification as follow:

\_\_\_\_\_  
\_\_\_\_\_  
-----  
Total Impurities: NMT (-----)

- e. Provide one time photostability data.
4. Provide three copies of method validation packages.

Please note that additional labeling comments will be provided shortly. If you have any questions, contact Ms. Sandy Barnes, Chief, Project Management Staff at 301-827-1055.

/s/

---

Ladan Jafari, Regulatory Project Manager

NDA 21-375

Page 3

Initialed by: Barnes/6-10-02  
KimCh/6-10-02  
Poochikian/6-10-02

Filename:N21375inforequest

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/s/

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Ladan Jafari  
6/11/02 09:44:22, AM  
CSO

**REQUEST FOR CONSULTATION**

TO (Division/Office): Office of Post Marketing Drug Risk Assessment, HFD-400

FROM: Anthony Zeccola, Project Manager, HFD-570

DATE June 6, 2002	IND NO.	NDA NO. 21-375	TYPE OF DOCUMENT BL	DATE OF DOCUMENT May 24, 2002
NAME OF DRUG loratidine		PRIORITY CONSIDERATION S	CLASSIFICATION OF DRUG 3SN	DESIRED COMPLETION DATE June 21, 2002

NAME OF FIRM: Wyeth Consumer Healthcare

**REASON FOR REQUEST**

**I. GENERAL**

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

**II. BIOMETRICS**

STATISTICAL EVALUATION BRANCH

- TYPE A OR B NDA REVIEW
- END OF PHASE II MEETING
- CONTROLLED STUDIES
- PROTOCOL REVIEW
- OTHER (SPECIFY BELOW):

STATISTICAL APPLICATION BRANCH

- CHEMISTRY REVIEW
- PHARMACOLOGY
- BIOPHARMACEUTICS
- OTHER (SPECIFY BELOW):

**III. BIOPHARMACEUTICS**

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

**IV. DRUG EXPERIENCE**

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

**V. SCIENTIFIC INVESTIGATIONS**

CLINICAL

PRECLINICAL

**COMMENTS/SPECIAL INSTRUCTIONS:** This is a 505(b)(2), direct to OTC NDA for loratidine. Although it is an OTC product, DPADP and DOTCDP would like OPRDA input on the proposed names, ALAVERT™ and Children's Dimetapp.

Wyeth, recently replaced the "Dimetapp" with "Children's Dimetapp". We are not sure what age group they will put in the "Direction". On 5/30/02, OTC informed Wyeth that we discourage the use of an existing popular brand name as the brandname for another active ingredient. This could cause confusion in the market place. Also the general thought here and in OTC is that we do not believe that we should approve two brand names in the same application targeting two populations (i.e., Alavert for children 6 and above to adults and Children's Dimetapp for children 6 to 11). The OTC Division requested that I note this in the consult request.

Please note that the entire submission can be found in EDR under NDA 21-375

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SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one) <input type="checkbox"/> MAIL <input type="checkbox"/> HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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

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Anthony Zeccola  
6/6/02 02:45:33 PM

**CONSULTATION RESPONSE**

**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT  
OFFICE OF DRUG SAFETY  
(DMETS, HFD-420)**

**DATE RECEIVED:** June 6, 2002

**DUE DATE:** July 2, 2002

**ODS CONSULT #:** 02-0132

**TO:** Badrul Chowdury, M.D.  
Acting Director, Division of Pulmonary and Allergy Drug Products  
HFD-570

**THROUGH:** Anthony Zeccola  
Project Manager  
HFD-570

**PRODUCT NAME:**  
Alavert (Adults & Children > 6 years of age)  
Children's Dimetapp (Children < 6 years of age)  
(Loratadine — Disintegrating Tablets) 10 mg

**NDA SPONSOR:**  
Wyeth Consumer Healthcare

**NDA:** 21-375

**SAFETY EVALUATOR:** Denise P. Toyer, Pharm.D.

**SUMMARY:** In response to a consult from the Division of Pulmonary and Allergy Drug Products (HFD-570), the Division of Medication Errors and Technical Support (DMETS) conducted a review of the proposed proprietary name "Alavert" to determine the potential for confusion with approved proprietary and established names as well as pending names.

**DMETS RECOMMENDATION:**

1. DMETS has no objections to the use of the proprietary name, Alavert.
2. DMETS does not recommend use of the name, Children's Dimetapp.

DMETS considers this a final review. However, if the approval of the NDA is delayed beyond 90 days from the date of this review, the name, labels and labeling must be re-evaluated. A re-review of the name before NDA approval will rule out any objections based upon approvals of other proprietary/established names from this date forward.

*JS*

*JS*

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Jerry Phillips, R.Ph.  
Associate Director  
Office of Drug Safety  
Center for Drug Evaluation and Research  
Food and Drug Administration

**Division of Medication Errors and Technical Support (DMETS)**  
**Office of Drug Safety**  
**HFD-420; Rm. 15B32**  
**Center for Drug Evaluation and Research**

**PROPRIETARY NAME REVIEW**

**DATE OF REVIEW:** July 3, 2002

**NDA#** 21-375

**NAME OF DRUG:** Alavert (Adults & Children > 6 years of age)  
Children's Dimetapp (Children < 6 years of age)  
(Loratadine) — Disintegrating Tablets 10 mg

**NDA HOLDER:** Wyeth Consumer Healthcare

**I. INTRODUCTION:**

This consult was written in response to a request from the Division of Pulmonary and Allergy Drug Products (HFD-570), for assessment of the tradename "Alavert," regarding potential name confusion with other proprietary drug names. The Alavert container labels/carton labeling and the Children's Dimetapp carton labeling (front panel only) were submitted and were reviewed for possible interventions in minimizing medication errors.

**PRODUCT INFORMATION**

Alavert and Childrens Dimetapp are the proposed proprietary names for loratadine 10 mg 1 — disintegrating tablets. Loratadine products are currently available by prescription only. The new drug application provides for over-the-counter (OTC) sales of loratadine 10 mg tablets. Loratadine is a long-acting tricyclic antihistamine with selective peripheral histamine H<sub>1</sub>-receptor antagonistic activity. Alavert is the proposed name for loratadine for adults and children older than 6 years of age. Childrens Dimetapp is the proposed name for loratadine for children less than 6 years of age. Wyeth Consumer Healthcare is proposing two different proprietary names for the same active ingredient for two different age populations. Both products are indicated for the relief of hay fever symptoms or symptoms related to other upper respiratory allergies (e.g., runny nose, sneezing, itchy and watery eyes, and itching of the nose or throat). The dosage regimen for both products is the same (i.e., 10 mg daily). However, Alavert will be indicated for adults and children older than 6 years of age whereas Childrens Dimetapp will only be indicated for children less than 6 years of age. The formulation of Alavert and Childrens Dimetapp is — disintegrating tablet, which — disintegrates when placed on the tongue. Patients may administer the — disintegrating tablet with or without water.

## II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts<sup>1,2</sup> as well as several FDA databases<sup>3</sup> for existing drug names which sound-alike or look-alike to “Alavert” to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office’s Text and Image Database was also conducted.<sup>4</sup> The Saegis<sup>5</sup> Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

### A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name “Alavert.” Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. The Expert Panel identified Salivart, Antivert, Elavil, Alacort, Alamast, and Alupent as having the potential for confusion with “Alavert.” These products are listed in Table 1 (see page 4), along with the dosage forms available and usual dosage.
2. The Expert Panel had concerns about the name Childrens Dimetapp due to the existing line of Dimetapp products that contain different active ingredients (i.e., brompheniramine maleate, pseudoephedrine, dextromethorphan, or acetaminophen).
3. DDMAC did not have concerns about the names Alavert or Childrens Dimetapp with regard to promotional claims.

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<sup>1</sup> MICROMEDEX Healthcare Intranet Series, 2000, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Index Nominum, and PDR/Physician’s Desk Reference (Medical Economics Company Inc, 2000).

<sup>2</sup> Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

<sup>3</sup> The Established Evaluation System [EES], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-00, and the electronic online version of the FDA Orange Book.

<sup>4</sup> WWW location <http://www.uspto.gov/tmdb/index.html>.

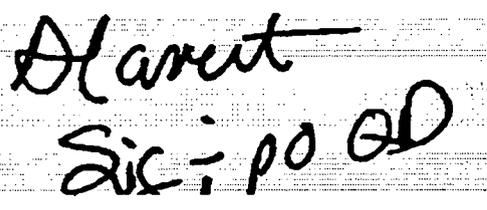
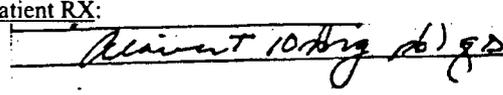
<sup>5</sup> Data provided by Thomson & Thomson’s SAEGIS™ Online Service, available at [www.thomson-thomson.com](http://www.thomson-thomson.com)

Table 1 Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel			
Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Alavert	Loratadine Rapidly Disintegrating 10 mg Tablets	10 mg daily	
Salivart	Sodium Carboxymethylcellulose 1% and Sorbital 3%	Spray as needed for dry mouth	SA/LA
Antivert	Meclozine 12.5 mg, 25 mg, and 50 mg Tablets	Vertigo: 25 mg to 100 mg daily in divided doses Motion Sickness 25 to 50 mg 1 hour before travel and daily for duration of travel	SA/LA
Elavil	Amitriptyline 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, and 150 mg Tablets. 10 mg/mL Injection	Initial: 75 mg to 100 mg per day in divided doses Maintenance 50 mg to 100 mg per day	SA
Alamast	Pemirolast Potassium Ophthalmic Solution 0.1%	One to two drops in eyes four times a day	LA
Alacort	Hydrocortisone Cream 1% or Hydrocortisone Lotion 1% and 2%	One to four times a day depending upon indication of use	LA
Alupent	Metaproterenol Sulfate 10 mg and 20 mg Tablets, 10 mg/5 mL Syrup	Tablets/Syrup: 10 mg to 20 mg three or four times a day	LA
*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike)			

## B. PRESCRIPTION ANALYSIS STUDIES

### 1. Methodology:

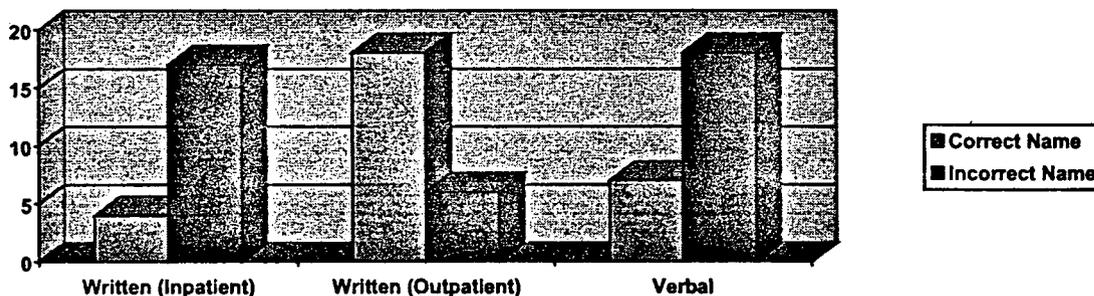
Three separate studies were conducted within FDA for the proposed proprietary name to determine the degree of confusion of "Alavert" with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 104 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for "Alavert" (see below). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretation and review. After receiving either the written or verbal prescription orders, the participants sent their interpretation of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p>Outpatient RX:</p> 	<p>...The third prescription is Alavert 1 po QD #10 ...</p>
<p>Inpatient RX:</p> 	

2. Results:

The results are summarized in Table II.

Study	# of Participants	# of Responses (%)	Correctly Interpreted	Incorrectly Interpreted
Written Inpatient	32	21 (66%)	4	17
Written Outpatient	36	24 (67%)	18	6
Verbal	36	25 (69%)	7	18
Total	104	70 (67%)	29	41



In the verbal study 18 of 25 (72%) participants interpreted “Alavert” incorrectly. All of the incorrect name interpretations were phonetic variations of “Alavert.” Alovert (6), Alivert (4), and Allovert (4) represented the majority of the incorrect interpretations. Other variations included Allavert (1), Alervert (1), Allavirt (1), and Ellevert (1). None of the misinterpreted names were similar to an approved product.

Among the two written studies, 23 of 45 (43%) participants interpreted the name incorrectly. Seven respondents misinterpreted the name as currently marketed

products—Antivert (2), Atrovent (2), Ativan T (1), Aldomet (1), and Darvocet (1). Additionally, two respondents misinterpreted the name as Atovert and Aluvent, phonetic versions of Atrovent and Alupent respectively. The remaining variations of "Alavert" were: Alavent (5), Alamet (2), Alarect (1), Havert (1), Aiavent (1), Alaivin T (1), Aliven T (1), Alivent (1), and Aravert (1). Alupent and Antivert were two of the names identified during the Expert Panel discussion as having the potential for name confusion.

### C. SAFETY EVALUATOR RISK ASSESSMENT

#### 1. Alavert

In reviewing the proprietary name Alavert, the primary concerns raised were related to several sound-alike and/or look-alike names: Salivart, Antivert, Elavil, Alamast, and Alupent.

Salivart is an over-the-counter product that is used to treat dry mouth and throat conditions. Although Salivart is an OTC product, it is often kept behind the pharmacy counter and must be asked for by patients. This product is supplied as a 75-gram aerosol spray can. The usual recommended dosing interval is 'as needed.' Although both Salivart and Alavert are OTC products, the differences (directions of use, strength, and dosing formulation) will minimize the potential of medication errors due to name confusion.

is a prescription hydrocortisone product that is available as a lotion (1% and 2%) and a cream (1%). Both products begin with the same prefix 'Ala' but end in different suffixes ( vs. vert). However, they may sound-alike when pronounced. and Alavert may also look similar when scripted (see below). However, there are several different factors that may decrease the potential for name confusion between these two products. The strength of the products (1% and 2% vs. 10 mg), route of administration (topical vs. oral), dosage formulation (cream and lotion vs. tablet), and availability (prescription vs. OTC) should all help to decrease the potential for name confusion between these products.

ALA-CORT

ALAVERT



Alamast is an ophthalmic eye drop used to prevent itching of the eye due to allergic conjunctivitis. Due to the same prefix 'Ala,' Alamast and Alavert may look-alike when scripted (see below). However, the differences should minimize name confusion between these products. Alamast is a solution whereas Alavert is an oral tablet. The dosing intervals (four times a day for Alamast and daily for Alavert), directions for use (instill vs. take), route of administration (topical vs. oral), strength (0.1% vs. 10 mg), and availability (prescription vs. OTC) are different and should decrease potential name confusion.

ALAMAST

ALAVERT

*Alupent Alavert*

Alupent is the another product that raised concerns relating to look-alike issues with Alavert. Both Alupent and Alavert are three syllable words that begin with the prefix 'Al.' The second ('u' vs. 'a') and third syllables ('pent' vs. 'vert') may look-alike. Overall, the names may look-alike when scripted (see below). Although Alupent is available as a tablet, syrup, metered dose inhaler, and inhalation solution; the formulation of most concern due to name confusion is tablets. The tablet formulation of Alupent has an overlapping strength with Alavert (10 mg). However, there are other distinguishing characteristics that may decrease the risk of medication errors between these two products. Alupent is prescribed three to four times a day depending on the dose whereas Alavert is prescribed once daily. Alupent tablets must be written with a strength (10 mg or 20 mg). Alavert is only available as a 10 mg tablet and the strength may be omitted when prescribed. Additionally, the majority of the patients taking Alupent tablets will also concurrently take some other type of anti-asthmatic drugs (e.g., inhalers). Although Alavert and Alupent share similar alphabetical characters, DMETS feels the last syllable of each name distinguishes the names from each other. Thus reducing the risk of name confusion. Moreover, the differences in dosing intervals (four times a day vs. once daily), availability (prescription vs. OTC), and the lack of a required strength for Alavert also helps to reduce the potential of medication errors due to name confusion.

**ALUPENT**

**ALAVERT**

*Alupent Alavert*

Elavil is a prescription-only tricyclic antidepressant. The Expert Panel identified Elavil as a sound-alike name for Alavert. Elavil tablets are available in various strengths ranging from 10 mg to 150 mg. The 'Ela' and 'Ala' beginning letters of each name may sound similar when pronounced. However, the endings are different (vil vs. vert). Elavil may be given in divided doses, but it may also be given once a day. Another similarity is the overlapping strengths (10 mg) between Elavil and Alavert. Additionally, the numerical strengths of Elavil and Alavert are similar (100 mg vs. 10 mg respectively). The Alavert strength may be misinterpreted as an Elavil strength, if the Alavert dose is written with a trailing zero (e.g., 10.0 vs. 10) and an undistinguished decimal point. However, Alavert may be written without a strength since it is available only as a 10 mg tablet. Prescriptions for Elavil will require a strength. The concern is that Elavil and Alavert may sound-alike when called into pharmacies by clinicians; however, since Alavert is an over-the-counter product most clinicians will give this information directly to patients and not call the prescription into a pharmacy. In a hospital setting clinicians will likely order the prescription product (Claritin) or use the product's established name. Although Alavert and Elavil sound similar, DMETS feels that the differences in combination with the differences in the last syllable of each name distinguishes the names from each other and thus reduces the potential for name confusion.

Antivert is a prescription-only, piperazine-derivative antihistamine that is used as an anti-emetic and in the treatment of vertigo. The usual recommended dose for dizziness is 25 mg to 100 mg daily in divided doses. For motion sickness the usual dose is 25 mg to 50 mg one hour before travel and daily for the duration of the trip. Antivert and Alavert are three syllable names that begin with the letter 'A' and end with the letters 'vert.' The similarities in characters contribute to the sound and look-alike characteristics of these two names. Both of these products are oral tablets. However, the differences between these two products may help to reduce the potential for name confusion. Antivert is available as a 12.5 mg, 25 mg, and 50 mg tablet whereas Alavert is only available as a 10 mg tablet. Although both products may be given once a day, when Antivert is prescribed for motion sickness, it is likely the directions for use will prompt patients to administer the medication one hour before traveling. Since Antivert is usually given more than once a day when treating dizziness, the potential for overlapping dosing intervals with Alavert is decreased. The dosing interval for dizziness is usually more than once a day. Alavert is only available in one strength, therefore the strength may be omitted from prescriptions. Prescriptions for Antivert will always require a strength to differentiate the dose. Two respondents in the prescription analysis studies misinterpreted the Alavert prescription as Antivert. Strength was not indicated on the test prescription and the practitioner would need to contact the prescriber prior to dispensing Antivert. Thus, the differences in strength and the fact that Alavert may be prescribed without a strength should help to minimize the potential for medication errors due to name confusion.

ANTIVERT

ALAVERT

*Antivert Alavert*

Respondents in the prescription analysis studies identified several currently marketed products as having the potential to look like Alavert. These products are: Atrovent (2), Aldomet (1), Darvocet (1), and Ativan T (1). Although, DMETS is concerned that the respondents thought Alavert looked similar to these currently marketed products, the differences between each of these products and Alavert reduces the potential for name confusion. Table three lists the products, with their appropriate strength, indication of use and recommended dosage regimen. None of the products have overlapping strengths with Alavert. Additionally, all of the products except Ativan, have different dosing regimens than Alavert. Although Ativan can be prescribed as 'once a day,' a strength of '10 mg' would usually warrant the healthcare practitioner to verify that the prescriber wanted such a high dose. Moreover, all of the products that are tablet formulations require that strength be noted whereas Alavert is available in one strength.

<b>Proprietary Name (Established Name)</b>	<b>Available Strength and Dosage Formulation</b>	<b>Usual Recommended Dosage</b>	<b>Indication of Use</b>
Atrovent	Nasal Spray 0.03% and 0.06%	2 Sprays each nostril TID or QID	Rhinorrhea
	Inhalation Solution 0.02%	500 mcg Q6 to 8 hours	Emphysema
	Metered Dose Inhaler 18 mcg	36 mcg QID	
Ativan T <sup>1</sup> (Lorazepam)	0.5 mg, 1 mg, and 2 mg Tablets	<i>Initially:</i> 2 mg to 3 mg daily in 2 to 3 divided doses, may increase to 2 mg to 6 mg daily in divided doses	Antianxiety
Aldomet (Methyldopa)	125 mg, 250 mg, and 500 mg Tablets	<i>Initially:</i> 250 mg BID or TID <i>Maintenance:</i> 500 mg to 2 gm daily (divided as BID to QID)	Hypertension
Darvocet N <sup>2</sup> (Propoxyphene Napsylate & Acetaminophen)	50 mg and 100 mg Tablets	100 mg every 4 hours as needed	Analgesia
1. Respondent listed an unused modifier 'T' 2. Respondent did not list the modifier 'N'			

## 2. Children's Dimetapp

Wyeth Consumer Healthcare proposes use of two proprietary names for the same active ingredient, loratadine. Alavert will be indicated for adults and children older than six years of age, whereas Children's Dimetapp will be indicated for children younger than 6 years of age. The products are identical and there is no pharmacological difference in the proposed products. DMETS does not recommend use of the proprietary name, Children's Dimetapp for the over-the-counter (OTC) loratadine product for children younger than 6 years of age. This concern is based on safety issues pertaining to two proprietary names for the same active ingredient by the same manufacturer and the fact that Dimetapp is a highly recognized proprietary name for a product line that predominantly contains pseudoephedrine in combination with brompheniramine maleate, acetaminophen, or dextromethorphan.

- Poison Control Centers and emergency practitioners will be unable to properly manage overdoses and accidental exposure to loratadine, when the reporter provides information pertaining to Children's Dimetapp. The management of exposure for pseudoephedrine, brompheniramine maleate, acetaminophen, and dextromethorphan might be different than for loratadine.
- Patients might inappropriately use (i.e., use the wrong dose or duration) the loratadine product expecting to be treated with Children's Dimetapp (pseudoephedrine, brompheniramine maleate, acetaminophen, and dextromethorphan).

DMETS has received medication error reports where consumers indicate potential confusion between products with the same proprietary name but different active ingredients. Attachment one contains a listing of some of these potential medication error reports.

### III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

In the review of the container labels and carton labeling of Alavert and Children's Dimetapp Allergy, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has reviewed the current container labels, carton and insert labeling and has identified several areas of possible improvement, which might minimize potential user error.

#### A. GENERAL

DMETS notes that the label and labeling identifies the dosing formulation as \_\_\_\_\_ Tablets.' \_\_\_\_\_ is not a recognized dosage form by the United States Pharmacopoeia (USP). We recommend consulting the CDER Labeling & Nomenclature Committee (LNC) for guidance.

#### B. ALAVERT - BLISTER FOIL LABEL

Relocate the established name so that it appears beneath the proprietary name and revise the dosage form "tablets" in the established name (i.e., Loratadine 10 mg. \_\_\_\_\_ Disintegrating Tablet) since each blister contains only one tablet.

#### B. ALAVERT - CARTON LABELING

1. The established name should appear beneath the proprietary name. Revise accordingly.
2. The established name as a part of the statement of identity should be increased to a size that is reasonably related to the proprietary name in accordance with CFR 201.61. Revise accordingly.

#### C. CHILDREN'S DIMETAPP - CARTON LABELING

\_\_\_\_\_  
\_\_\_\_\_

#### **IV. RECOMMENDATIONS:**

DMETS has no objections to the use of the proprietary name Alavert.

DMETS does not recommend use of the proprietary name Children's Dimetapp.

DMETS considers this a final review. However, if the approval of the NDA is delayed beyond 90 days from the date of this review, the name, labels, and labeling must be re-evaluated. A re-review of the name before NDA approval will rule out any objections based upon approvals of other proprietary/established names from this date forward.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sammie Beam, project manager, at 301-827-3242.

/s/

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Denise P. Toyer, Pharm.D.  
Safety Evaluator  
Division of Medication Errors and Technical Support  
Office of Drug Safety

**ATTACHMENT ONE**

AERS/DQRS Accession Number	Date Received	Narrative
3680163-6	03/14/01	<b>UNISOM</b> name confusion. Two different drug products sold under the same name by the same manufacturer.
3698813-7	03/19/01	Two generics marketed under the same brand name. No incident, but confusion and potential incident. Bayer markets two Nasal <b>NEO-SYNEPHRINE</b> brand products: One is "Neo-Synephrine 12 Hour Nasal Spray." The other is "Neo-Synephrine Regular Nasal Spray". The former contains oxymetazoline 0.05%. The later contains phenylephrine 0.5%. Two generics marked under the same brand name. Also Neo-Synephrine is so closely aligned with phenylephrine, no one would imagine that if they buy, prescribe, dispense, or administer Neo-Synephrine, it might be oxymetazoline.
U-15907	10/17/92	This complaint is mainly with the FDA for allowing a drug company to change product formulations in a way that will be apt to deceive customers, and is confusing at best. For years there was an <b>ANUSOL</b> ointment and there was and Anusol HC Cream, with 1% Hydrocortisone. Now there is not Anusol HC Cream with the old formula. There is still a plain Anusol, but the product labeled "Anusol-HC 1" has no Anusol in it.
M-122403	07/17/96	See attached letter regarding confusion between <b>BETADINE</b> Ointments containing either PVP Iodine or else Polymixin B and Bacitracin. Reporter is concerned about frequent confusion between two products with virtually the same name but different ingredients. The name "Betadine" has always referred to a line of products whose chief ingredient is PVP Iodine. A relatively new product has been introduced which contains Polymixin B and Bacitracin, and is referred to as clear Betadine.
U-42116	10/10/96	Manufacturer has two products with the same name but different ingredients. <b>BOROFAX</b> Topical Ointment contains 5% Boric Acid and Borofax Skin Protectant contains 5% Zinc Oxide. This similarity in names can cause the wrong product to be selected without realizing that the desired actions are different.
M-123890	02/23/97	OTC 8 hour product has 8 mg of <b>CHLORPHENIRAMINE</b> . OTC 4 hour product has 4 mg Chlorpheniramine and 60 mg of Pseudoephedrine. This is misleading labeling. This could present a problem with patient who have BP problems and they by the product that contains Pseudoephedrine.
M-121851	05/01/96	Reporter is writing to express concern about the labeling for <b>CHLORTRIMETON</b> brand of Pseudoephedrine sold by Schering-Plough. The name "Chlortrimeton" has, for many years, been closely associated with Chlorpheniramine. The association has been so close that the terms are now used interchangeably. When people wish to recommend Chlorpheniramine, they occasionally say "Chlortrimeton". When patients with hypertension, coronary or peripheral vascular disease want OTC medicine to treat upper respiratory infections, reporter often suggests Chlorpheniramine. For some of these patients, Pseudoephedrine could do harm. Reporter's concern is that someone with sever hypertension could grab a box of "Chlortrimeton" thinking hat it was Chlorpheniramine, take Pseudoephedrine instead, and have an adverse event as a result.

<b>M-123860</b>	02/20/97	Product name is misleading: <b>DIABETIC TUSSIN EX</b> = Guaifenesin, Diabetic Tussin DM = Guaifenesin plus Dextrometorphan, Diabetic Tussin Allergy Relief = Chlorpheniramine Maleate. One would be lead to believe the product contains Guaifenesin.
<b>U-50421</b>	08/21/97	Ads state " <b>EXCEDRIN Aspirin-Free</b> " but there are Excedrin products with Aspirin. May confuse consumers.
<b>M-123868</b>	02/21/97	Who approves drug names at FDA? It is done without any regard for patient safety. <b>MYLANTA AR</b> is the next accident waiting to happen. Allowing manufacturers to use a brand name for an entirely different product just by adding a suffix is stupid and dangerous.
<b>U-40262</b>	04/26/95	The reporter is concerned about the product's name change. Some confusion has occurred between <b>MYLANTA</b> and Mylanta Gas.
<b>D-121460</b>	03/20/96	<b>NEO-SYNEPHRINE</b> Nasal Spray and Drops as well as the injectable form is the brand name for Phenylephrine HCl. Apparently in the fall of 1994, a 12 hour spray was developed with the use of Oxymetazoline 0.05%. The name Neo-Synephrine was used for this new application. Oxymetazoline is on the package label in very small type. People who are allergic or who may have had a bad reaction to Oxymetazoline but not to Phenylephrine might purchase the new 12-hour spray inadvertently and not realize that it is a totally different product. Another potential problem would be if the user was used to the more frequent Neo-Synephrine products and starts to use Oxymetazoline more often than recommended.
<b>D-121920</b>	05/09/96	Report received on USP Veterinary Practitioner's Reporting form. Owner was sent to purchase <b>NEO-SYNEPHRINE 0.125%</b> (phenylephrine) Nasal Spray. Owner purchased Neo-Synephrine but it contained oxymetazoline. Poorly named product. Name implies Phenylephrine.
<b>U-50268</b>	06/25/97	The name of this new product, <b>TAVIST Sinus</b> (shipping will begin in August), implies that it will contain the same ingredient as other Tavist products. This will cause problems with consumers, especially those with little knowledge of medical products, when they unknowingly consume a product they believe to be Tavist (clemastine fumarate) and is, in fact, Pseudoephedrine and acetaminophen.
<b>U-41995</b>	07/08/96	<b>TYLENOL PM</b> might be misunderstood to be just another form of regular Tylenol rather than Tylenol that has an antihistamine, diphenhydramine, in it. The PM label might give patients and/or consumers the idea that the product is just plain Tylenol that works better in the evening comparison to regular Tylenol.
<b>D-124378</b>	05/14/97	Reporter relayed his concerns for the name of these two products ( <b>UNIFED</b> and Uni fed). These are 2 different products with different ingredients, but have the same name. Unifed is a liquid containing pseudoephedrine HCl and Uni Fed is a syrup (and tablet) that contains Triprolidine 2.5 mg and pseudoephedrine 60 mg. This could cause confusion.
<b>U-19669</b>	06/23/94	<b>Unisom</b> contains 25 mg of doxylamine succinate. <b>Unisom Plus</b> pain relief contains two other ingredients but no doxylamine succinate. The reporter stated that because of confusing names of these products and many others, every day thousands of patients are taking the wrong medications.

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/s/

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Denise Toyer  
7/3/02 01:03:42 PM  
PHARMACIST

Carol Holquist  
7/3/02 01:42:10 PM  
PHARMACIST

Jerry Phillips  
7/3/02 02:39:47 PM  
DIRECTOR



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

**FACSIMILE TRANSMITTAL SHEET**

**DATE:** May 16, 2002

<b>To:</b> David S. Smith, Ph.D.	<b>From:</b> Elaine Abraham
<b>Company:</b> Wyeth Consumer Healthcare	Division of Over-the-Counter Drug Products
<b>Fax number:</b> (973) 660-8698	<b>Fax number:</b> (301) 827-2315
<b>Phone number:</b> (973) 660-6806	<b>Phone number:</b> (301) 827-2293
<b>Subject:</b> non-drowsy <del>          </del> claims	

**Total no. of pages including cover:** 2

**Comments:**

**Document to be mailed:**       YES       NO

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-2222. Thank you.

**Message:** Please refer to your new drug application NDA 21-375 dated August 23, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Alavert Allergy/Dimetapp Allergy (loratadine 10 mg orally disintegrating tablets).

We have attached reviewer's comments related to the non-drowsy and  claims in the labeling submitted. In order to ensure a timely action for this new drug application, we request that you respond to the issues listed below as soon as possible. You can fax your response to Elaine Abraham at (301) 827-2315.

**1. Non-Drowsy claim**

The incidence of drowsiness when taking 10 mg loratadine is significantly less than the incidence of somnolence when taking antihistamine drug products currently available over-the-counter. However, the incidence of drowsiness when taking loratadine at the labeled dose is of particular concern for some consumers, particularly those with hepatic or renal impairment and the elderly, or those on medications that impair clearance of loratadine and its metabolites. Further, if consumers take more than the recommended dose, sedation may occur. These concerns are stated in the current prescription labeling for loratadine drug products.

Because the proposed claims of "Non-drowsy" and "...without causing drowsiness" are not absolute for all consumers, we seek proposals from you on how best to communicate in the OTC labeling of these products the relative nature of the claim of "non-drowsiness."

2.

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

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/s/

-----  
Elaine Abraham  
5/17/02 07:39:47 AM  
CSO

## Memorandum of Telephone Facsimile Correspondence

Date: 04/11/02

To: Sharon C.Heddish  
Vice President, Regulatory Affairs

From: Anthony Zeccola  
Regulatory Management Officer  
Division of Pulmonary Drug Products  
FDA

Subject: Request for Information – NDA 21-375

Total Pages: 2

We are providing the attached information via telephone facsimile for your convenience, to expedite the progress of your drug development program. This material should be viewed as unofficial correspondence. Please feel free to contact me if you have any questions regarding the contents of this transmission.

**THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.** If you are not the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you received this document in error, please immediately notify us by telephone at (301) 827-1050 and return it to us at 5600 Fishers Lane, HFD-570, DPDP, Rockville, MD 20857.

Thank you.

*/s/*

---

Anthony M. Zeccola  
Regulatory Management Officer  
Division of Pulmonary Drug Products

Please provide the following information to assist in our review of NDA 21-375, these requests pertain to studies 99-104-MA and 99-105-MA:

Subject 5 dropped from the study prior to Phase 2 dosing [hpbio\bio\99104ma.pdf, page 14]. This subject reported an adverse event (AE) for lightheadedness [hpbio\bio\99104ma.pdf, page 23]. Subject 126 dropped from the study prior to Phase 2 dosing [hpbio\bio\99104ma.pdf, page 14]. This subject reported AEs for skin rash, Strep throat, and sore throat [hpbio\bio\99104ma.pdf, page 25].

1. Did these patients withdraw from the study because of their AEs?
2. Please provide narratives and case report forms for these patients if they withdrew from the study because of the AEs. of adverse events should be provided.

**APPEARS THIS WAY  
ON ORIGINAL**

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/s/

-----  
Anthony Zeccola  
4/11/02 04:39:32 PM  
CSO

## Memorandum of Telephone Facsimile Correspondence

Date: December 6, 2001  
To: David Smith  
Whitehall-Robins Healthcare  
Fax No.: 973-660-7187  
From: David Hilfiker  
Project Manager  
Subject: Information Request  
# of Pages: 2

We are providing the attached information request via telephone facsimile to expedite the progress of your drug development program. Please feel free to contact me if you have any questions regarding the contents of this transmission.

**THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.** If you are not the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you received this document in error, please immediately notify us by telephone at (301) 827-1050 and return it to us at 5600 Fishers Lane, HFD-570, DPDP, Rockville, MD 20857.

Thank you.

Dr. Smith:

We have determined that there are no deficiencies to your NDA that would preclude it from being accepted for filing. However, we have identified several items that are needed to adequately evaluate your application. These items are listed below:

- Your analysis of the publicly available safety data for loratadine did not include subgroup analyses, for certain patient populations such as geriatric and renally or hepatically impaired patients. Provide such analyses to your NDA.
- You did not specify in the NDA what your plans are for pediatric development of this formulation. If it is your intention not to study patients less than 12 years of age, you should submit a request for partial waiver of the requirement to studies patients under 12 years of age, as per 21 CFR 314.55. Otherwise, submit a general investigational plan for studies in patients below 12 years of age.
- Submit labeling (text translated where appropriate) from other countries where loratadine is marketed over-the-counter.

If you have any questions regarding these requests, contact Mr. Tony Zeccola, Regulatory Management Officer, at (301) 827-1058. Please note that I will be leaving the Division of Pulmonary and Allergy Drug Products effective December 10, and will be starting a new work assignment within the Division of Over-the-Counter Drug Products. It has been a pleasure working with you.

Dave Hilfiker  
Regulatory Project Manager

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/s/

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David Hilfiker

12/6/01 09:27:00 AM

CSO

Fax transmittal successful, 10:19 am, 12-6-01

## REQUEST FOR CONSULTATION

(Division/Office): **HFD-400/OPDRA/Associate Director for Medication Error Prevention**

FROM: **HFD-570/DPADP/Hilfiker**

DATE: November 27, 2001	IDA NO.:	NDA NO.: <b>21-375</b>	TYPE OF DOCUMENT: Original NDA	DATE OF DOCUMENT: N/A
----------------------------	----------	---------------------------	-----------------------------------	--------------------------

NAME OF DRUGS: <b>Alavert and Dimetapp Allergy</b>	PRIORITY CONSIDERATION: standard	CLASSIFICATION OF DRUG: 3S	DESIRED COMPLETION DATE: <b>January 30, 2001</b>
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NAME OF FIRM: **Whitehall Robins Healthcare**

### REASON FOR REQUEST

#### I. GENERAL

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

#### II. BIOMETRICS

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

#### III. BIOPHARMACEUTICS

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

#### IV. DRUG EXPERIENCE

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

#### V. SCIENTIFIC INVESTIGATIONS

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

**COMMENTS/SPECIAL INSTRUCTIONS:** This new NDA was submitted in August for the approval of an OTC version of 10 mg loratadine orally disintegrating tablets (currently marketed by Schering Corp. as Claritin Reditabs). The applicant has proposed marketing this product under two separate tradenames, Dimetapp Allergy and Alavert. As an OTC product, FDA does not normally have jurisdiction to regulate the proposed tradename and packaging materials. However, the Division of Pulmonary and Allergy Drug Products and Division of Over the Counter Drug Products feel that the use of two different tradenames could lead to consumer confusion and potential medication errors, especially in an unsupervised OTC setting.

We are seeking the OPDRA opinion on the proposed use of two different OTC tradenames and its implication for the safe use of this product in the marketplace. See attached proposed labeling (taken from the original NDA).

SIGNATURE OF REQUESTER: (Hilfiker)	METHOD OF DELIVERY (Check one): <input checked="" type="checkbox"/> MAIL <input type="checkbox"/> HAND
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10 page(s) of  
revised draft labeling  
has been redacted  
from this portion of  
the review.

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/s/

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David Hilfiker  
11/27/01 02:52:32 PM

Robert Meyer  
11/29/01 11:26:42 AM

## ADMINISTRATIVE REVIEW FOR NDA 21-375

**Drug Product:** 10 mg loratadine hydrochloride orally disintegrating tablets  
**Indication:** OTC marketing for temporary relief of symptoms of hay fever and other upper respiratory allergies  
**Applicant:** Whitehall-Robins Healthcare  
**Contact:** David Smith  
**Phone:** 973-660-7187

**Letter Date:** August 23, 2001  
**Receipt Date:** September 4, 2001  
**Filing Date:** November 3, 2001  
**Action Date:** July 4, 2002

### Background

The concept of a switch in marketing status from prescription to over-the-counter for the antihistamines loratadine, cetirizine, and fexofenadine was discussed at a joint meeting of the Nonprescription Drug Advisory Committee and the Pulmonary and Allergy Drug Advisory Committee on May 11, 2001. The joint panel voted in favor of such a switch.

The Division held a pre-NDA meeting with Whitehall Robins on February 28, 2001, to discuss the requirements for filing a 505(b)(2) NDA for OTC marketing of a 10 mg loratadine orally disintegrating tablet. A follow-up teleconference was held on July 25, 2001, to discuss the proposed stability dataset for the NDA.

A separate teleconference was held on September 13, 2001, to discuss the requirements for 505(b)(2) NDAs for other loratadine dosage forms for OTC marketing.

NDA 21-375 was submitted by Whitehall Robins for the OTC marketing of a 10 mg loratadine orally disintegrating tablet. The application was submitted as a 505(b)(2), with reference to the FDA findings of safety and effectiveness for Claritin RediTabs (10 mg loratadine orally disintegrating tablets), marketed as a prescription product under NDA 20-704 by Schering Corporation. The FDA has determined that a 505(b)(2) NDA is a viable route for approval of the Rx-to-OTC switch of a drug product when the data supporting the drug product is not fully owned by the applicant nor does the applicant have right of reference to such data.

NDA 21-375 consists of a comprehensive review of the publicly available information with regard to the safety of loratadine in an OTC setting and two clinical study reports to demonstrate that the proposed product is comparably bioavailable to the reference listed drug (Claritin RediTabs). Much of the safety and effectiveness information is incorporated by way of reference to the FDA's previous finding of safety and effectiveness for the RLD NDA 20-704.

### **Review Team Assignments**

Clinical	Charles Lee
Clinical Pharmacology and Biopharmaceutics	Shinja Kim
Statistics	N/A
Pharmacology/Toxicology	Lawrence Sancilio
CMC	Chong-Ho Kim

### **Electronic Submission**

WHR has submitted the archival copy as an electronic document, according to the Guidance for Industry entitled "Providing Regulatory Submissions in Electronic Format – NDAs." The only paper copy that was submitted for archival purposes was a cover letter, signed Form 356h, and signed user fee cover sheet with a copy of the user fee payment.

Deficiency: WHR did not provide archival paper copies of all documents that require original signatures, including the debarment statement, patent certification, financial disclosure form, and field copy certification, as stipulated in the current Guidance for Industry.

Comment: WHR claims to have included a version of the proposed label in MS Word, but this file was not found in the electronic submission.

### **Labeling**

WHR has submitted proposed OTC carton labeling in the Drug Facts format codified in 21 CFR 201.66.

### **Exclusivity Claims**

WHR has not submitted a claim for exclusivity. In the February 28 meeting, FDA informed WHR that exclusivity would not likely be granted for the types of clinical data submitted in this application.

### **Pediatric Information and Exclusivity**

WHR proposes the use of this product down to 6 years of age, consistent with the innovator prescription NDA. WHR has not requested a waiver or deferral of pediatric studies (as per 21 CFR 314.55) for children under the age of 6 years, and has not proposed a pediatric development plan for this age range.

**Debarment Certification**

WHR submitted a debarment statement certifying that all persons that have a contribution to this NDA are not debarred at stipulated under Section 306 of the FD&C Act.

Deficiency: The debarment statement is not in conformance with the required language under subsection 306(k) of the FD&C Act. This subsection prohibits language such as the use of \_\_\_\_\_

**User Fees**

Appropriate user fees were received as of August 7, 2001.

**Patent Certification**

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

**Financial Disclosure of Clinical Investigators**

WHR submitted a completed Form 3454 for certification of the financial interests of investigators who participated in Studies 99-104-MA and 99-105-MA.

Deficiency: In the cover letter of the submission, WHR claimed not to be the sponsor of the clinical investigations submitted to this NDA. (Wyeth-Ayerst Pharmaceuticals, another subsidiary of American Home Products Corporation, was identified as the sponsor.) But on the Form 3454, WHR checked statement 1, appropriate for applicants who were the sponsor for the submitted clinical investigations. WHR is considered to be

the applicant but not the sponsor of the clinical investigations, for the purposes of this form.

### **General Organization**

The archival NDA consists of one paper volume and one CD containing the electronic media. The paper volume does not include the necessary forms and certifications with original signatures, as mentioned above.

Paper review copies were submitted for the Clinical, Human Pharmacokinetics and Bioavailability, and CMC sections of the NDA. Each section begins with volume 1, to be consistent with the electronic archival submission. Each review discipline was provided with a copy of the administrative volume as well, also labeled volume 1. The administrative volume contains an overall table of contents for the NDA. Volume 1 of each review volume set contains a table of contents for the review volume set.

### Comments

In the Clinical review volume set, the table of contents in volume 1 refers to a compilation of the publications submitted in support of the application in volume 2 of the set. However, no volume 2 was submitted.

In the human Pharmacokinetics and Bioavailability review volume set, the table of contents for the review volume set refers to study report 99-104-MA starting in volume 2, when it actually begins in volume 1 of the set. Likewise, the table of contents for the review volume set refers to the assay methodology used for the submitted BA/BE studies being in volume 3 of the set, when these methods are located in volume 4 of the set.

### **CONCLUSIONS**

The NDA is deficient from an administrative standpoint with respect to the following components:

- Patent certification
- Financial disclosure
- Debarment statement
- Field copy certification

I contacted David Smith of WHR on September 27, 2001, and conveyed all of the deficiencies and comments noted in this review. He agreed to supplement the paper archival volume submitted to the NDA with the necessary corrected information. Dr. Smith also agreed to submit paper review volume 2 for the Clinical section and revised tables of contents for the Clinical and Human PK and BA sections to the paper review copies of the NDA.

Given that these deficiencies can be rectified within a reasonable time frame, the NDA should be fileable from an administrative standpoint.

Draft by: HFD-570/Hilfiker/9-28-01

Concurrence: HFD-570/Barnes/10-30-01

C:\data\my documents\N21375\010928adminrev

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/s/

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David Hilfiker  
10/30/01 02:18:07 PM  
CSO

Memorandum of Telephone Facsimile Correspondence

Date: March 13, 2001  
To: David Smith  
Fax: 973-660-7162  
From: Gretchen Trout  
Project Manager  
Subject: pre-IND  
February 28, 2001 meeting

Reference is made to the meeting held between representatives of your company and the Agency on February 28, 2001. Attached is a copy of our final minutes for the meeting. These minutes will serve as the official record of the meeting. If you have any questions or comments regarding the minutes, please call me at (301) 827-1058.

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Thank you.

10 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

# NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information		
NDA 21-375	Efficacy Supplement Type SE-	Supplement Number
Drug: Alovera™ (loratidine) Orally Disintegrating Tablets		Applicant: Wyeth Consumer Healthcare
RPM: Zeccola	HFD-570	Phone # 827-1058
Application Type: ( ) 505(b)(1) (X) 505(b)(2)		Reference Listed Drug (NDA #, Drug name):
❖ Application Classifications:		
• Review priority		(X) Standard ( ) Priority
• Chem class (NDAs only)		3
• Other (e.g., orphan, OTC)		N
❖ User Fee Goal Dates		04-July-2002
❖ Special programs (indicate all that apply)		(X) None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review
❖ User Fee Information		
• User Fee		(X) Paid
• User Fee waiver		( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other
• User Fee exception		( ) Orphan designation ( ) No-fee 505(b)(2) ( ) Other
❖ Application Integrity Policy (AIP)		
• Applicant is on the AIP		( ) Yes (X) No
• This application is on the AIP		( ) Yes (X) No
• Exception for review (Center Director's memo)		
• OC clearance for approval		
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification and certifications from foreign applicants are co-signed by U.S. agent.		(X) Verified
❖ Patent		
• Information: Verify that patent information was submitted		(X) Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted		21 CFR 314.50(i)(1)(i)(A) ( ) I ( ) II (X) III ( ) IV  21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).		( ) Verified

<b>Exclusivity (approvals only)</b>	
<ul style="list-style-type: none"> <li>Exclusivity summary</li> </ul>	
<ul style="list-style-type: none"> <li>Is there an existing orphan drug exclusivity protection for the active moiety for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of sameness for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification!</i></li> </ul>	<input type="checkbox"/> Yes, Application # _____ <input type="checkbox"/> No
❖ Administrative Reviews (Project Manager, ADRA) (indicate date of each review)	
<b>General Information</b>	
❖ Actions	
<ul style="list-style-type: none"> <li>Proposed action</li> </ul>	<input type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA
<ul style="list-style-type: none"> <li>Previous actions (specify type and date for each action taken)</li> </ul>	
<ul style="list-style-type: none"> <li>Status of advertising (approvals only)</li> </ul>	<input type="checkbox"/> Materials requested in AP letter <input type="checkbox"/> Reviewed for Subpart H
❖ Public communications	
<ul style="list-style-type: none"> <li>Press Office notified of action (approval only)</li> </ul>	<input type="checkbox"/> Yes <input type="checkbox"/> Not applicable
<ul style="list-style-type: none"> <li>Indicate what types (if any) of information dissemination are anticipated</li> </ul>	<input type="checkbox"/> None <input type="checkbox"/> Press Release <input type="checkbox"/> Talk Paper <input type="checkbox"/> Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable))	
<ul style="list-style-type: none"> <li>Division's proposed labeling (only if generated after latest applicant submission of labeling)</li> </ul>	
<ul style="list-style-type: none"> <li>Most recent applicant-proposed labeling</li> </ul>	X
<ul style="list-style-type: none"> <li>Original applicant-proposed labeling</li> </ul>	X
<ul style="list-style-type: none"> <li>Labeling reviews (including DDMAC, Office of Drug Safety trade name review, nomenclature reviews) and minutes of labeling meetings (indicate dates of reviews and meetings)</li> </ul>	
<ul style="list-style-type: none"> <li>Other relevant labeling (e.g., most recent 3 in class, class labeling)</li> </ul>	
❖ Labels (immediate container & carton labels)	
<ul style="list-style-type: none"> <li>Division proposed (only if generated after latest applicant submission)</li> </ul>	
<ul style="list-style-type: none"> <li>Applicant proposed</li> </ul>	X
<ul style="list-style-type: none"> <li>Reviews</li> </ul>	
❖ Post-marketing commitments	
<ul style="list-style-type: none"> <li>Agency request for post-marketing commitments</li> </ul>	
<ul style="list-style-type: none"> <li>Documentation of discussions and/or agreements relating to post-marketing commitments</li> </ul>	
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	
❖ Memoranda and Telecons	
❖ Minutes of Meetings	
<ul style="list-style-type: none"> <li>EOP2 meeting (indicate date)</li> </ul>	
<ul style="list-style-type: none"> <li>Pre-NDA meeting (indicate date)</li> </ul>	
<ul style="list-style-type: none"> <li>Pre-Approval Safety Conference (indicate date, approvals only)</li> </ul>	
<ul style="list-style-type: none"> <li>Other</li> </ul>	

<b>Advisory Committee Meeting</b>	
• Date of Meeting	
• 48-hour alert	
❖ Federal Register Notices, DESI documents, NAS, NRC (if any are applicable)	
<b>Summary Application Review</b>	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) <i>(indicate date for each review)</i>	
<b>Clinical Information</b>	
❖ Clinical review(s) <i>(indicate date for each review)</i>	
❖ Microbiology (efficacy) review(s) <i>(indicate date for each review)</i>	<del>Not</del> Not Needed
❖ Safety Update review(s) <i>(indicate date or location if incorporated in another review)</i>	6/10/02
❖ Pediatric Page (separate page for each indication addressing status of all age groups)	
❖ Statistical review(s) <i>(indicate date for each review)</i>	Not needed
❖ Biopharmaceutical review(s) <i>(indicate date for each review)</i>	
❖ Controlled Substance Staff review(s) and recommendation for scheduling <i>(indicate date for each review)</i>	Not needed
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	Not Requested
• Bioequivalence studies	
<b>CMC Information</b>	
CMC review(s) <i>(indicate date for each review)</i>	
❖ Environmental Assessment	
• Categorical Exclusion <i>(indicate review date)</i>	6/10/02
• Review & FONSI <i>(indicate date of review)</i>	—
• Review & Environmental Impact Statement <i>(indicate date of each review)</i>	—
❖ Micro (validation of sterilization & product sterility) review(s) <i>(indicate date for each review)</i>	NOT NEEDED
❖ Facilities inspection (provide EER report)	Date completed: ( ) Acceptable ( ) Withhold recommendation
❖ Methods validation	( ) Completed ( ) Requested ( ) Not yet requested
<b>Nonclinical Pharm/Tox Information</b>	
❖ Pharm/tox review(s), including referenced IND reviews <i>(indicate date for each review)</i>	
❖ Nonclinical inspection review summary	—
❖ Statistical review(s) of carcinogenicity studies <i>(indicate date for each review)</i>	—
❖ CAC/ECAC report	—