CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

20-786 /S002

Trade Name: Allegra-D

Generic Name: fexofenadine HCl/pseudoephedrine

Sponsor: Aventis Pharmaceuticals

Approval Date: December 21, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-786 /S002

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	X
Approvable Letter	
Labeling	
Summary Review	
Officer/Employee List	
Office Director Memo	
Cross Discipline Team Leader Review	
Medical Review(s)	
Chemistry Review(s)	X
Environmental Assessment	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/Biopharmaceutics Review(s)	X
Risk Assessment and Risk Mitigation Review(s)	
Proprietary Name Review(s)	
Administrative/Correspondence Document(s)	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-786 /S002

APPROVAL LETTER

NDA 20-786/S-002

DEC 2 1 1999

Hoechst Marion Roussel
10236 Marion Park Drive
P.O. Box 9627
Kansas City, MO 64134-0627

Attention: J. Michael Nicholas, Ph.D.
Director, Marketed Products
Regulatory Affairs

Dear Dr. Nicholas:

Please refer to your supplemental new drug application dated June 19, 1998, received June 22, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Allegra-D (fexofenadine hydrochloride and pseudoephedrine hydrochloride) Extended-Release Tablets.

We acknowledge receipt of your submissions dated July 15, October 27, and November 30, 1998, February 26, March 29, April 8, 12, and 23, May 27, June 11, 14, 17, and 24, July 7, 15, and 21, August 20, 27, and 31, September 16 and 27, October 1, 4, 7, 8, 13, 14, 15, 20, 25, and 29, November 9, 11, 15, 16, 17, 22, and 30, December 6, 9, and 16. Your submission of August 31, 1999, constituted a complete response to our August 6, 1999, action letter.

This supplemental new drug application provides for the following changes.

1. Controlling pseudoephedrine hydrochloride drug substance [redacted] specification.

2. Deletion of [redacted] specification for the pseudoephedrine hydrochloride drug substance.

3. Deletion [redacted] specifications for the pseudoephedrine hydrochloride drug substance.

4. Addition of [redacted] pseudoephedrine hydrochloride.

5. Withdrawal of [redacted] pseudoephedrine hydrochloride.

We have completed the review of this supplemental application, as amended, and it is approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Mrs. Gretchen Trout, Project Manager, at (301) 827-1058.

Sincerely yours,

Guirag Poochikian, Ph.D.
Chemistry Team Leader
Division of Pulmonary and Allergy Drug Products, HFD-570
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

cc:
Archival NDA 20-786
HFD-570/Div. Files
HFD-570/G.Trout
HFD-570/Rogers
HFD-570/Poochikian
HFD-570/Choi
HFD-570/Uppoor
HFD-095/DDMS-IMT
HFD-820/DNDC Division Director
DISTRICT OFFICE

BMR 12/21/99
GST 12-21-99

Drafted by: GST/December 20, 1999
Initialed by: Barnes/12-20-99
Choi/12-20-99
Rogers/12-20-99
Bertha (for Poochikian)/12-20-99 BfoCP 12/21/99

final: GTrout/12-21-99
filename: n:\staff\troutg\20786ap

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-786 /S002

CHEMISTRY REVIEW(S)

31.1

DEC 20 1999

CHEMIST'S REVIEW

1. ORGANIZATION	2. NDA NUMBER
HFD-570 DPDP	20-786

3. NAME AND ADDRESS OF APPLICANT (City and State)	4. AF NUMBER	5. SUPPLEMENT(S) NUMBER	DATE
Hoechst Marion Roussel, Inc. PO Box 9627 Kansas City, MO 64134-0627		SCS-002	6/19/98

6. NAME OF DRUG	7. NONPROPRIETARY NAME
Allegra-D™ Extended-release Tablets	fexofenadine hydrochloride and pseudoephedrine hydrochloride extended-release tablets

8. SUPPLEMENT PROVIDES FOR:

1. Controlling pseudoephedrine HCl drug substance [redacted] specification
2. Deletion of [redacted] specification for the pseudoephedrine HCl drug substance
3. Deletion [redacted] specifications for the pseudoephedrine HCl drug substance
4. Addition [redacted] pseudoephedrine HCl
5. Withdrawal [redacted] pseudoephedrine HCl

9. AMENDMENT(S), REPORT(S), ETC.

SCS-002 BC*	10/4/99
SCS-002 BC*	10/4/99
SCS-002 BC*	11/9/99
SCS-002 BC*	11/11/99
SCS-002 BC*	11/15/99
SCS-002 BC*	11/16/99
SCS-002 BC*	11/17/99
SCS-002 BC*	11/17/99
SCS-002 BC*	11/17/99
SCS-002 BC*	11/22/99
SCS-002 BC*	11/22/99
SCS-002 BC*	11/22/99
SCS-002 BC*	11/30/99
SCS-002 BC*	12/6/99
SCS-002 BC*	12/6/99
SCS-002 BC*	12/6/99
SCS-002 BC*	12/6/99
SCS-002 BC*	12/9/99
SCS-002 BC*	12/17/99

*Subject of this review. See comments (Item 17) below for additional submissions

10. PHARMACOLOGICAL CATEGORY	11. HOW DISPENSED	12. RELATED IND/NDA/DMF
Histamine H_1-receptor antagonist/decongestant for treatment of symptoms associated with seasonal allergic rhinitis	RX X OTC __	

13. DOSAGE FORM(S)	14. POTENCY
Extended-release Tablet	60 mg immediate-release fexofenadine hydrochloride and 120 mg extended-release pseudoephedrine hydrochloride

15. CHEMICAL NAME AND STRUCTURE	16. RECORDS AND REPORTS
(±)-4-[1-Hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]-dimethylbenzeneacetic acid HCl and [S-(R*,R*)]-α-[1-(Methylamino)ethyl]-benzenemethanol HCl (for structures see USAN)	CURRENT YES_ NO_ REVIEWED YES_ NO_

17. COMMENTS: Based upon 11/5/99 meeting comments from Y-Y Chiu, approval of this supplement must be de-coupled from any outstanding GMP issues pertaining to [redacted]. An Acceptable EES rating will not be required for [redacted] as a condition for approval of this supplement. Additional amendments (BC) were dated 7/15/98, 10/27/98, 11/30/98, 2/22/99, 2/26/99, 3/29/99, 4/8/99, 4/12/99, 4/12/99, 4/19/99, 4/19/99, 4/19/99, 4/21/99, 4/21/99, 4/21/99, 4/23/99, 4/26/99, 4/26/99, 4/29/99, 4/29/99, 4/30/99, 4/30/99, 5/3/99, 5/3/99, 5/4/99, 5/4/99, 5/4/99, 5/4/99, 5/4/99, 5/25/99, 5/27/99, 6/3/99 6/11/99, 6/14/99, 6/17/99, 6/24/99, 7/7/99, 7/15/99, 7/21/99, 8/17/99, (AC) 8/20/99, 8/27/99, 8/27/99, (AZ) 8/31/99, 9/16/99, 9/16/99, 9/27/99, 10/1/99, 10/1/99, 10/7/99, 10/8/99, 10/13/99, 10/14/99, 10/14/99, 10/15/99, 10/20/99, 10/25/99, 10/29/99, and 10/29/99.

cc:
Orig. NDA #20-786
HFD-570/div. File
HFD-570/BRogers/12/20/99
HFD-570/GPoochikian
HFD-570/GTrout
R/D Init. by: CB for GP 12/20/99
F/T by: B. Rogers/12/20/99
doc # 20786.c02.DOC

18. CONCLUSIONS AND RECOMMENDATIONS: The supplement is APPROVED.

19. REVIEWER NAME	20. SIGNATURE	21. DATE COMPLETED
Brian D. Rogers, Ph.D.	Brian D. Rogers	12/20/99

7 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 20-786 S002

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-786/S002

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

NOV 20 1998

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW

NDA 20,786 S-002 SUBMISSION DATE: October 27, 1998

DRUG NAME AND FORMULATION: Allegra-D tablets (fexofenadine hydrochloride/pseudoephedrine hydrochloride extended release tablets)

SPONSOR: Hoechst Marion Russell, Inc., Kansas City, MO 64134-0627

REVIEWER: Venkata Ramana S. Uppoor, Ph.D.

TYPE OF SUBMISSION: Drug substance process change

BACKGROUND: Allegra-D contains immediate release fexofenadine and extended release pseudoephedrine. This drug is currently on the market as a combination product of antihistamine and decongestant. The sponsor is currently developing a [redacted] for the pseudoephedrine drug substance (resulting in an average [redacted] an average [redacted] and an average [redacted]). The process change involves only the drug substance of pseudoephedrine and not drug product. Previously the sponsor was requested to provide comparative dissolution profiles comparing the [redacted] pseudoephedrine to the [redacted] submitted in the NDA.

OBJECTIVE: This submission contains the dissolution data [redacted] on the [redacted] produced with the [redacted] process for pseudoephedrine. In addition, it also contains [redacted] which will be reviewed by the chemist.

CURRENT SUBMISSION: In this package, the sponsor submitted dissolution data ([redacted]) in 4 dissolution media, 0.001N HCl (approved medium), pH 1.2 simulated gastric fluid, pH 4.5 phosphate buffer and pH 6.8 simulated intestinal fluid. [redacted] of pseudoephedrine drug substance [redacted] that was [redacted] according to the new process was used to manufacture the Allegra-D tablets [redacted] Dissolution data from the [redacted] was also provided. F2 values were computed to compare the dissolution profiles.

Dissolution data is shown in the following tables:

DISSOLUTION IN 0.001 N hydrochloric acid (approved medium):

Lot #	Average [redacted] pseudoephedrine dissolved								F2 value
	15 min	30 min	45 min	60 min	180 min	300 min	420 min	720 min	
[redacted]									52.8
									56.4

DISSOLUTION IN pH 1.2 SIMULATED GASTRIC FLUID WITHOUT ENZYME:

Lot #	Average [redacted] % pseudoephedrine dissolved								F2 value
	15 min	30 min	45 min	60 min	180 min	300 min	420 min	720 min	
									51.1
									57.1

DISSOLUTION IN pH 4.5 PHOSPHATE BUFFER:

Lot #	Average [redacted] % pseudoephedrine dissolved								F2 value
	15 min	30 min	45 min	60 min	180 min	300 min	420 min	720 min	
									52.5
									55.9

DISSOLUTION IN pH 6.8 SIMULATED INTESTINAL FLUID WITHOUT ENZYME:

Lot #	Average [redacted] % pseudoephedrine dissolved								F2 value
	15 min	30 min	45 min	60 min	180 min	300 min	420 min	720 min	
									44.7
									46.7

F2 values for fexofenadine in all dissolution media tested were greater than 50. Please note that no process change has been made to the fexofenadine entity.

COMMENT: While dissolution profiles for pseudoephedrine appear to be different in the intestinal fluid, f2 values were close to 50. In addition to this dissolution data, the average % dissolved values were still within the approved dissolution specifications for Allegra-D (for fexofenadine, Q = [redacted] % in [redacted] minutes, for pseudoephedrine, at [redacted] minutes – NMT [redacted] at [redacted] minutes – [redacted] %, at [redacted] minutes - [redacted] %, and at [redacted] minutes – NLT [redacted]). Further, since pseudoephedrine is a base, some variability is expected in dissolution in basic media.

CONCLUSION: Generally for a process change for a drug substance, one only compares dissolution profiles in the approved dissolution medium. Since the dissolution profiles are comparable for the batches produced with the [redacted] process for pseudoephedrine and [redacted] in the approved dissolution medium, this change is acceptable.

RECOMMENDATION:

This submission has been reviewed by the Office of Clinical Pharmacology and Biopharmaceutics. Data provided is found to be acceptable for the process change in

the pseudoephedrine drug substance from Biopharmaceutics' point of view.

11/20/98

Venkata Ramana S. Uppoor, Ph.D.
Division of Pharmaceutical Evaluation - II

FT Initialed by Mei-Ling Chen, Ph.D. 11/20/98

CC list: HFD-570: NDA 20,786; Division file; Lindsay Cobbs; Rogers; HFD-870: Venkata Ramana S. Uppoor; Mei-Ling Chen, John Hunt, HFD-850: Lesko; CDR: Attn: Barbara Murphy/Trout

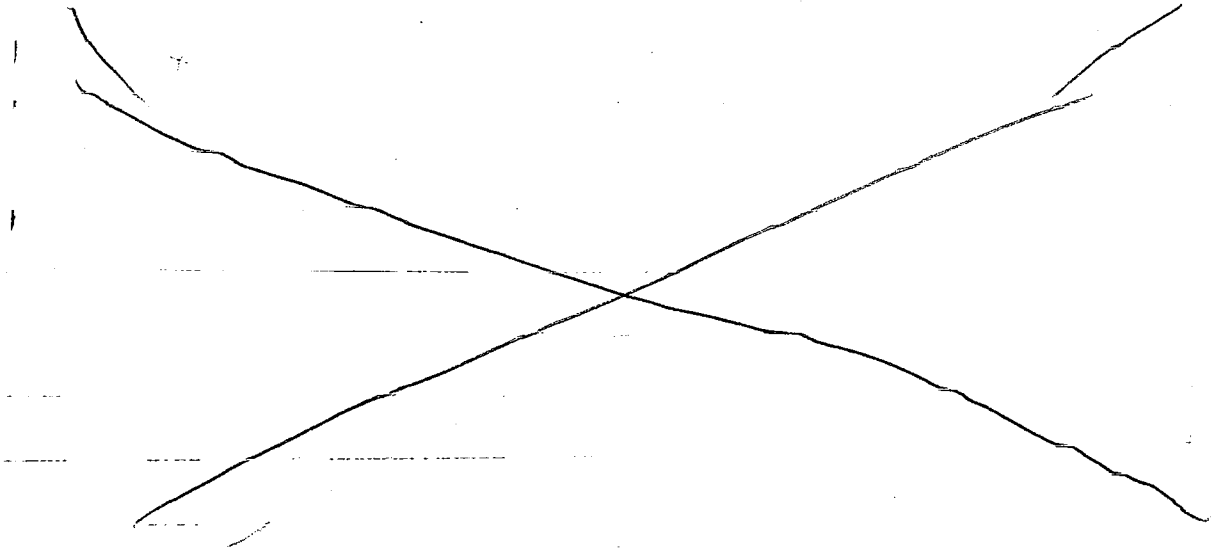
Hoechst Marion Roussel, Inc.

NDA 20-786

ALLEGRA-D™
(combination fexofenadine hydrochloride 60 mg and pseudoephedrine hydrochloride 120 mg tablets)

List of Referenced Documents

Type	Number	Title/Subject	Holder	Reference
IND	43,573	Fexofenadine HCl	Hoechst Marion Roussel Inc.	Entire File
NDA	20-625	Fexofenadine HCl	Hoechst Marion Roussel Inc.	Entire File



[1] Letter of Access

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-786 /S002

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

MEMORANDUM OF TELECON

DATE: July 14, 1998

NDA: 20-786/S-002

PRODUCT: Allegra-D (fexofenadine HCl and pseudoephedrine HCl)

PARTICIPANTS:

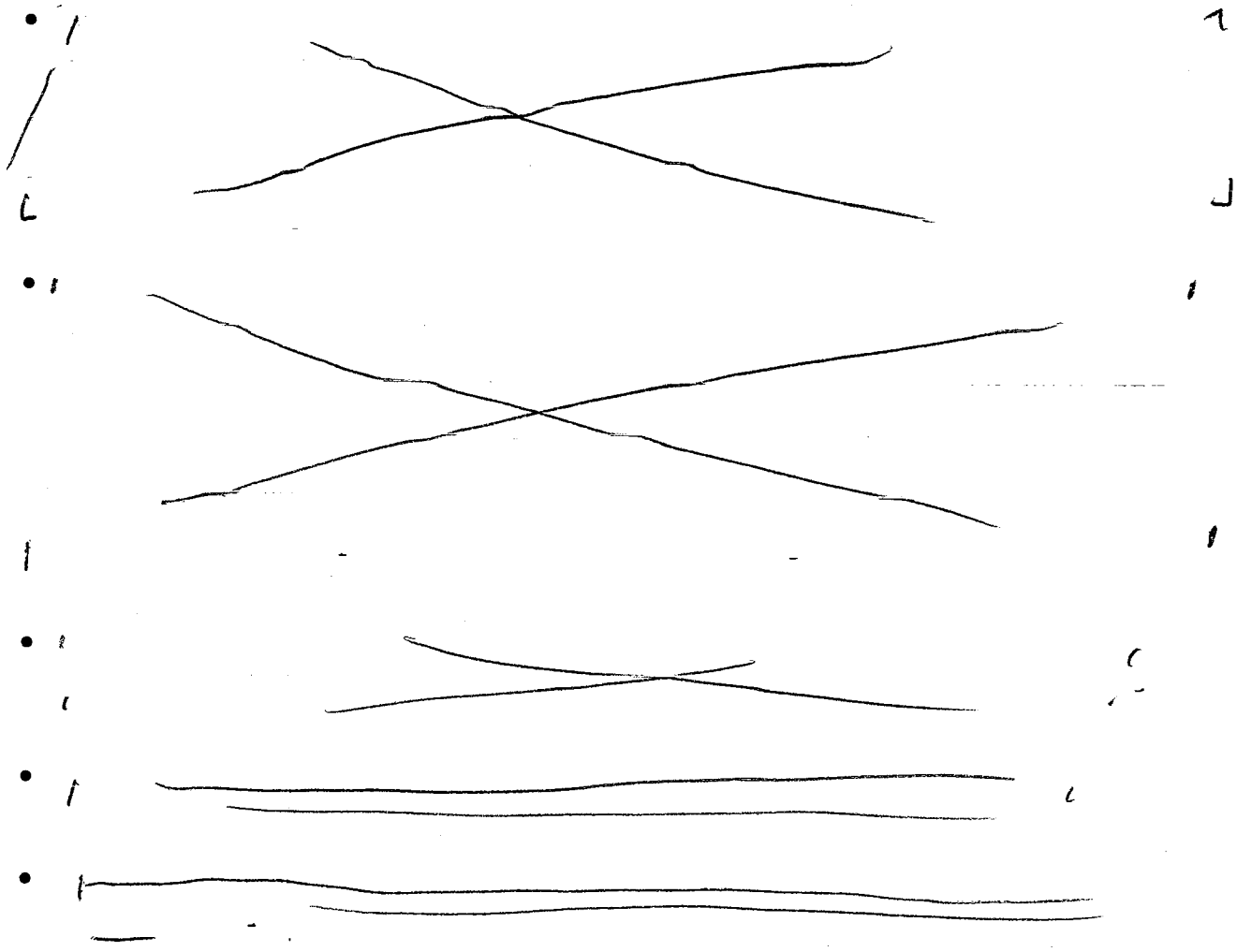
FDA:	Karl Lin	Biometrics Reviewer
	Brian Rogers	Chemistry Reviewer
	Gretchen Trout	Project Manager
HMR:	Dave Maclaren	CMC
	Dhiren Shah	Regulatory Affairs
	Gary Silvey	CMC

BACKGROUND: The Division requested this teleconference to discuss issues with regard to supplement 002 (S-002) which provides for a new [redacted] method and a new specification for pseudoephedrine HCl.

The Division questioned if HMR has looked at the tablets through a multivarient analysis. HMR replied that they have not formally done a multivarient analysis. [redacted] factor effecting dissolution [redacted] is [redacted] HMR looked at a [redacted] and a [redacted] There is an [redacted] change in dissolution from the [redacted]

The Division referred to S-002 wherein HMR [redacted] however the data [redacted] The Division is trying to understand what factors are really causing the dissolution problem. HMR stated that [redacted] The Division agreed that with [redacted] the data look better, however we would be looking at a specification of [redacted] microns at [redacted] HRM stated that [redacted] and [redacted] is the most accurate and has the best correlation. Specifications at [redacted] The Division replied that since [redacted] would seem to provide the most control.

The Division proposed that HMR conduct a multivarient analysis, and discussion followed on different factors which the Division might like to see used for the multivariant analysis (factors which might effect dissolution).



- [redacted] pseudoephedrine drug substance.
- [redacted]

The Division wants to see, for any of the batches that HMR has on stability, the drug product variables [redacted] The Division questioned if they [redacted] on stability. HMR replied that they [redacted]

The Division is concerned that if we set specifications, and a [redacted] HMR stated that they feel that the pseudoephedrine [redacted]

HMR said that the specifications should be set pseudoephedrine specifications. HMR said that for specifications. They would rather have tighter specifications . They specifications at

CONCLUSION:

HMR and the Division discussed a range of specifications, and HMR agreed that they could accept the following PROPOSED specifications (amended as per a follow-up conversation):

The Division will discuss these proposed specifications internally and decide if they are acceptable. The Division again encouraged

The Division also questioned if HMR

FOLLOW-UP:

In a follow-up teleconference on July 14, 1998, between Brian Rogers (FDA) and Dhiren Shah (HMR), Dr. Rogers informed Dr. Shah that the Division proposes changing the specification for pseudoephedrine dissolution to at min from in addition to the proposal discussed earlier with him concerning changes in specifications. Dr. Rogers suggested that Dr. Shah discuss this proposal internally. Dr. Rogers explained that the specification change would only be instituted at Dr. Shah stated that HMR currently has an for pseudoephedrine dissolution and he would discuss this proposal with others. Upon further discussion at a later time, Dr. Shah proposed that the at minutes. Dr. Rogers agreed that this is a reasonable proposal and will discuss it internally.

Dr. Rogers also requested that HMR send any [redacted] whose data were included in the facsimile dated January 14, 1998.

Gretchen Trout
Project Manager

cc: NDA 20-786
Div. File
HFD-570/Rogers
HFD-715/Lin
HFD-570/Trout
HFD-570/Poochikian
HFD-570/Gillespie

drafted: GST/July 15, 1998/n:\staff\troutg\20786.tel

rd initial by: Rogers/7-16-98

TELECONFERENCE

NDA 20-786/S-002

JUL 17 1998

Hoechst Marion Roussel
10236 Marion Park Drive
P.O.Box 9627
Kansas City, MO 64134-0627

Attention: Dhiren N. Shah, Ph.D.
Director
CMC, US Drug Regulatory Affairs

Dear Dr. Shah:

Please refer to your pending June 19, 1998, supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Allegra-D (fexofenadine HCl and pseudoephedrine HCl) Tablets.

We are reviewing your submission and have the following comment and information request:

In order to ensure the comparability of Allegra-D product with the you should compare a in three dissolution media (simulated gastric fluid, pH 4.5 buffer and simulated intestinal fluid). Complete dissolution versus time profiles of the should be compared statistically using the f2 test procedure. The used for comparison with must be manufactured with pseudoephedrine HCl which is must also pass the proposed

We would appreciate your prompt written response so we can continue our evaluation of your supplemental application.

These comments are being provided to you prior to completion of our review of the application to give you preliminary notice of issues that have been identified. Per the user fee reauthorization agreements, these comments have been reviewed only to the level of the discipline team leader. They do not reflect division director input or concurrence and should not be construed to do so. These comments are subject to change as the review of your application is finalized. In addition, we may identify other information that must be provided prior to approval of this application. If you respond in the current review cycle we

may or may not consider your response prior to taking an action on your application. In the meantime, we are continuing our review of your application.
If you have any questions, contact Ms. Gretchen Trout, Project Manager, at (301) 827-1058.

Sincerely yours,

Guirag Poochikian, Ph.D.
Chemistry Team Leader for
Division of Pulmonary Drug Products, (HFD-570)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

cc:
Archival NDA 20-786
HFD-570/Div. Files
HFD-570/Trout
HFD-570/Schumaker/7-17-98
HFD-570/Gillespie/7-17-98
HFD-570/Rogers/7-17-98
HFD-570/Poochikian/7-17-98
HFD-820/DNDC Division Director (only for CMC related issues)
DISTRICT OFFICE

Drafted by: PJani/July 17, 1998

Initialed by: BRogers/7-17-98 7/17/98 7/17/98
CSchumaker/7-17-98

Final Typed by: MStickell/July 17, 1998 7/17/98

filename: N207862.IR

INFORMATION REQUEST (IR)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-786/S-002

JUN 30 1998

HOECHST MARION ROUSSEL, INC.
PO BOX 9627
MARION PARK DRIVE
KANSAS CITY, MO 64134-0627

Attention: DHIREN N. SHAH, PH.D
DIRECTOR, CMC US DRUG REGULATORY AFFAIRS

Dear DR. SHAH:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: ALLEEGRA-D TABLETS

NDA Number: 20-786

Supplement Number: S-002

Date of Supplement: JUNE 19, 1998

Date of Receipt: JUNE 22, 1998

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on AUGUST 21. 1998 in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Pulmonary Drug Products, HFD-570
Office of Drug Evaluation II
Attention: Document Control Room 10B-03
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

for Cathie Schumaker
Chief, Project Management Staff
Division of Pulmonary Drug Products, HFD-570
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Original NDA 20-786/002
HFD-570/Div. Files
HFD-570/CSO/GRETCHEN TROUT

filename:

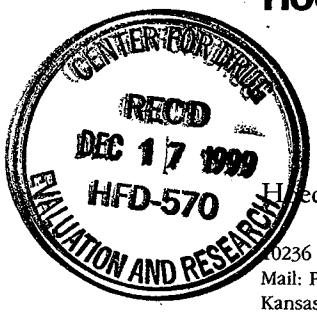
SUPPLEMENT ACKNOWLEDGEMENT

BC
SCS-002

NDA SUPP AMEND
ORIGINAL

Hoechst Marion Roussel

December 16, 1999



Hoechst Marion Roussel, Inc.
10236 Marion Park Drive
Mail: P.O. Box 9627
Kansas City, MO 64134-0627
Telephone (816) 966-5000
U.S. Web site: www.hmri.com

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Pulmonary Drug Products
(HFD-570)
5600 Fishers Lane
Rockville, MD 20857

Attention: Ms. Gretchen Trout, Regulatory Health Project Manager

Sent via Telefax: 301-827-1271

Re: NDA 20-786/S-002
ALLEGRA-D® Tablets
(fexofenadine HCl/pseudoephedrine HCl extended release tablets)

Amendment to Supplement
Chemistry, Manufacturing and Controls
Information for Teleconference on
December 17, 1999

Dear Ms. Trout:

Hoechst Marion Roussel hereby submits a proposed modification to the [redacted] for Allegra-D tablets and pseudoephedrine HCl (attached) for agency's consideration at the planned teleconference on December 17, 1999 at 10 AM (EST).

A paper copy of this telefax will be submitted today.

Should you have any comments or questions, please contact the undersigned at (816) 966-7104.

Sincerely,
Hoechst Marion Roussel, Inc.
Mail Station H3-M2112

Dhiren N. Shah

Dhiren N. Shah, Ph.D.
Director - CMC, US Drug Regulatory Affairs

2 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Administrative- 20-786
5002

ORIGINAL

Hoechst Marion Roussel

October 27, 1998

NDA SUPPL NEW AMEND
S-002

Hoechst Marion Roussel, Inc.

10236 Marion Park Drive
Mail: P.O. Box 9627
Kansas City, MO 64134-0627
Telephone (816) 966-5000
U.S. Web site: www.hmri.com

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Pulmonary Drug Products
(HFD-570)
Document Control Room 10B-45
5600 Fishers lane
Rockville, MD 20857

Attention: Dr. G. Poochikian, Chemistry Team Leader

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
OCT 29 1998
HFD-570

Re: NDA 20-786/S-002
Allegra-D Tablets
(fexofenadine HCl/pseudoephedrine HCl extended release tablets)

Amendment:
Chemistry, Manufacturing, and Controls
Additional Information

Dear Dr. Poochikian:

Please refer to the telephone conversations between Dr. B. Rogers of your review division and the undersigned on September 29, 1998 regarding the above-referenced supplement. In the phone conversation you had requested Hoechst Marion Roussel, Inc. (HMRI) to provide dissolution data on a [redacted] of Allegra-D manufactured with pseudoephedrine HCl which was [redacted]

HMRI hereby provides, in duplicate, an amendment to the supplement. This submission contains 1 volume.

The purpose of the amendment is to provide additional information on the [redacted] pseudoephedrine hydrochloride and dissolution data on the [redacted] that pseudoephedrine HCl. Additional data from [redacted] of Allegra-D tablets are also included in this submission.

Based on the information provided in the attachment, HMRI concludes the following:

- [redacted]

Hoechst

Hoechst Marion Roussel
The Pharmaceutical Company of Hoechst

- [redacted]

  pseudoephedrine HCl:
  - [redacted]
  - [redacted]
  - [redacted]
- As a result of the [redacted] pseudoephedrine HCl, we are able to [redacted] fexofenadine HCl.

We trust that we have satisfactorily addressed the pseudoephedrine HCl [redacted] HMRI acknowledges the input from the review division and especially by Dr. B. Rogers in resolving this issue.

Pursuant to 21 CFR 314.71(b), an exact copy of this submission has been sent to the Kansas City District Office.

Should you have any comments or questions, please contact the undersigned at (816) 966-7104.

Sincerely,
Hoechst Marion Roussel, Inc.
Mail Station H3-M2112

Dhiren N. Shah, Ph.D.
Director - CMC, US Drug Regulatory Affairs

Attachment

cc: Kansas City District Office, 11630 W. 80th Street, Lenexa, KS 66214