CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 16-126 / S-020

Name:	Primatene Mist Inhalation Aerosol
Sponsor:	Wyeth Consumer Healthcare
Approval Date:	November 24, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 16-126 / S-020

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Approved Labeling	
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Medical Review(s)	
Chemistry Review(s)	X
Statistical Review(s)	
Microbiology Review(s)	
Administrative Document(s)	X
Correspondence	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 16-126 / S-020

APPROVAL LETTER

NDA 16-126/S-020

Whitehall-Robins
Five Giralda Farms
Madison, NJ 07940-0871

Attention: Ken Warner
Director, Regulatory Affairs CMC

Dear Mr. Warner:

Please refer to your supplemental new drug application dated August 22, 1997, received August 25, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Primatene Mist (epinephrine) Inhalation Aerosol.

We acknowledge receipt of your submissions dated August 28, 1998, January 8 and June 30, 1999. Your submission of June 30, 1999, constituted a complete response to our March 1, 1999, action letter.

This supplemental new drug application provides for specifications and test methods for chlorofluorocarbons used in the drug product.

We have completed the review of this supplemental application 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 Ms. Parinda Jani, Project Manager, at (301) 827-1050.

Sincerely yours,

Guirag Poochikian, Ph.D.
Chemistry Team Leader for
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 16-126
HFD-570/Div. Files
HFD-570/Jani
HFD-570/Schroeder
HFD-570/Poochikian
HFD-560/Merritt
HFD-560/Ganley
HFD-095/DDMS-IMT
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: HFD-570/Hilfiker/11-24-99
Final: HFD-570/Hilfiker/11-24-99
Filename: c:\my_documents\N16126\S020\99-11-24.apltr.doc

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 16-126 / S-020

APPROVABLE LETTER(S)

NDA 16-126/S-020

Whitehall-Robins Healthcare
5 Giralda Farms
Madison, New Jersey 07940-0871

Attention: Ken Warner
Associate Director
Regulatory Affairs

Dear Mr. Warner:

Please refer to your supplemental new drug application dated August 22, 1997, received August 25, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Primatene Mist (epinephrine) Inhalation Aerosol.

We acknowledge receipt of your submissions dated August 28, 1998, and January 8, 1999. Your submission of August 28, 1998, constituted a complete response to our action letter.

This supplemental application provides for analytical methods, methods validation data and specifications for impurities in each CFC propellant.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to address the following:

1.

2.

3.

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16-126/S-020 APPROVABLE LETTER

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with these changes prior to approval of this supplemental application.

If you have any questions, contact Parinda Jani, Project Manager, at (301) 827-1064.

Sincerely yours,

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

cc:
Archival NDA 16-126
HFD-570/Div. files
HFD-820/ONDC Division Director
DISTRICT OFFICE
HFD-92/DDM-DIAB
HFD-570/P.Jani
HFD-570/Schroeder/2-26-99
HFD-570/Poochikian/2-26-99
HFD-570/Schumaker/2-26-99
HFD-560/Merritt
HFD-560/Cook
HFD-830/DD/Dunn

Drafted by:pj /February 26, 1999/
Initialed by:GPoochgikian
final:janip/3-1-99
filename: c:\my documents\n16126ae.020

APPROVABLE (AE)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 16-126 / S-020

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW #3	1. ORGANIZATION HFD-820	2. NDA NUMBER 16-126
3. NAME AND ADDRESS OF APPLICANT (City and State) Whitehall-Robins, Five Giralda Farms, Madison, NJ 07940-0871		4. AF NUMBER
		5. SUPPLEMENT (S) NUMBER(S) DATES(S)
6. NAME OF DRUG Primatene Mist	7. NONPROPRIETARY NAME epinephrine inhalation aerosol	SCM-020 8/22/97
8. SUPPLEMENT PROVIDES FOR: analytical methods, methods validation data and specifications for impurities in each CFC propellant.		9. AMENDMENTS DATES 6/30/99 (AC)* *Subj. of this review
10. PHARMACOLOGICAL CATEGORY bronchodilator	11. HOW DISPENSED RX _____ OTC X	12. RELATED IND/NDA/DMF
13. DOSAGE FORM(S) metered dose inhaler	14. POTENCY 0.22 mg epinephrine (base) per inhalation	
15. CHEMICAL NAME AND STRUCTURE See USP		16. RECORDS AND REPORTS CURRENT YES ____ NO ____ REVIEWED YES ____ NO ____

17. COMMENTS

cc:
Orig. NDA #16-126
HFD-560/Div. File
HFD-570/ACSchroeder/11-23-99
HFD-570/GPoochikian
HFD-570/CSO PJani
HFD-570/SJohnson
HFD-560/BMerritt
R/D Init. by:_____
F/T by: ACSchroeder/11-23-99
doc #N16126R3_S20.doc

18. CONCLUSIONS AND RECOMMENDATIONS

This supplement should be approved. Project Manager should prepare an approval letter.

19. REVIEWER

NAME	SIGNATURE	DATE COMPLETED
Alan C. Schroeder, Ph.D.		11/23/99

DISTRIBUTION ORIGINAL JACKET ___ DIVISION FILE ___ REVIEWER ___ CSO ___ SUP. CHEMIST ___

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16-126/S-020 CHEMISTRY REVIEW #3

CHEMIST'S REVIEW #2	1. ORGANIZATION HFD-570/820 DPDP	2. NDA NUMBER 16-126
3. NAME AND ADDRESS OF APPLICANT (City and State) Whitehall-Robins, Five Giralda Farms, Madison, NJ 07940-0871		4. AF NUMBER 5. SUPPLEMENT (S) NUMBER(S) DATES(S)
6. NAME OF DRUG Primatene Mist	7. NONPROPRIETARY NAME epinephrine inhalation aerosol	SCM-020 8/22/97
8. SUPPLEMENT PROVIDES FOR: analytical methods, methods validation data and specifications for impurities in each CFC propellant (CFC 12 and CFC 114).		9. AMENDMENTS DATES (AC) 8/28/98* (BC) 1/8/99* *subject of this review
10. PHARMACOLOGICAL CATEGORY bronchodilator	11. HOW DISPENSED RX _____ OTC X	12. RELATED IND/NDA/DMF
13. DOSAGE FORM(S) metered dose inhaler	14. POTENCY 0.22 mg epinephrine (base) per inhalation	
15. CHEMICAL NAME AND STRUCTURE See USP		16. RECORDS AND REPORTS CURRENT YES ____ NO ____ REVIEWED YES ____ NO ____

17. COMMENTS

cc:
Orig. NDA #16-126
HFD-570/Div. File
HFD-570/ACSchroeder/2-23-99
HFD-570/GPoochikian
HFD-570/CSO PJani
HFD-570/SJohnson
R/D Init. by:_____
F/T by: ACSchroeder/2-23-99
doc #N16126R2_S20.doc

18. CONCLUSIONS AND RECOMMENDATIONS

This supplement should be considered to be approvable, pending satisfactory response to the comments at the end of this review. The EER for the analytical laboratory was found to be satisfactory by our Office of Compliance on 5/8/98.

19. REVIEWER

NAME	SIGNATURE	DATE COMPLETED
Alan C. Schroeder, Ph.D.		2/23/99

DISTRIBUTION ORIGINAL JACKET ___ DIVISION FILE ___ REVIEWER ___ CSO ___ SUP. CHEMIST ___

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16-126/S-020 CHEMISTRY REVIEW #2

CHEMIST'S REVIEW

1. ORGANIZATION HFD-570 DPDP		2. NDA NUMBER 16-126
3. NAME AND ADDRESS OF APPLICANT (City and State) Whitehall-Robins, Five Giralda Farms, Madison, NJ 07940-0871		4. AF NUMBER
		5. SUPPLEMENT (S) NUMBER(S) DATES(S)
6. NAME OF DRUG Primatene Mist	7. NONPROPRIETARY NAME epinephrine inhalation aerosol	SCM-020 8/22/97
8. SUPPLEMENT PROVIDES FOR: analytical methods, methods validation data and specifications for impurities in each CFC propellant.		9. AMENDMENTS DATES
10. PHARMACOLOGICAL CATEGORY bronchodilator	11. HOW DISPENSED RX _____ OTC X	12. RELATED IND/NDA/DMF
13. DOSAGE FORM(S) metered dose inhaler	14. POTENCY 0.22 mg epinephrine (base) per inhalation	
15. CHEMICAL NAME AND STRUCTURE See USP		16. RECORDS AND REPORTS CURRENT YES ___ NO ___ REVIEWED YES ___ NO ___

17. COMMENTS

cc:
Orig. NDA #16-126
HFD-570/Div. File
HFD-570/ACSchroeder/2-5-98
HFD-570/GPoochikian
HFD-570/CSO PJani
HFD-570/SJohnson
R/D Init. by:_____
F/T by: ACSchroeder/2-5-98
doc #N16126R1_S20.doc

18. CONCLUSIONS AND RECOMMENDATIONS

This supplement should be considered to be "not approvable." The project manager should prepare a letter and include the chemistry deficiencies and comments at the end of this review. Note that an EER is pending.

19. REVIEWER

NAME	SIGNATURE	DATE COMPLETED
Alan C. Schroeder, Ph.D.		2/5/98

DISTRIBUTION ORIGINAL JACKET ___ DIVISION FILE ___ REVIEWER ___ CSO ___ SUP. CHEMIST ___

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16-126/S-020 CHEMISTRY REVIEW #1

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 16-126 / S-020

ADMINISTRATIVE DOCUMENTS

Record of Telephone Conversation

Date: June 17, 1999
Subject: NDA 16-126
Initiated by: FDA
Product Name: Primatene Mist Inhalation Aerosol
Firm Name: Whitehall-Robins Healthcare
Contact: Mr. Ken Warner
Telephone Number: (973) 660-6896

This telecon was in response to questions in a fax from the applicant (received 4/12/99) - see attachment to this memo.

I stated that this issue has been unresolved for a number of years; I expressed our significant concern that it should be resolved soon. (It isn't clear why it is taking so long to respond.) Mr. Warner stated that they were in agreement that it should be resolved soon. He stated that the specifications in the draft MDI/DPI guidance are different than the ones they had previously been given by the Agency; now that they have the specifications desired by the Agency they will move quickly on S-020. They anticipate replying to the outstanding S-020 issues (re: CFC impurity methods and specifications) by the beginning of July, 1999. They understand that S-017 (stockpiling at ———) will not be approved prior to approval of S-020. The supplement for CFC specifications and test methods is the most important and needs to be approved before CFC stockpiling or blending supplements can be approved.

Mr. Warner assured us that they have already implemented the tighter specifications for CFC propellants.

I agreed that they may (for S-017) cross-reference information provided in other supplements.

They feel they have a problem in that their CFC supplier does not wish to provide additional information or do additional testing. I said that we'd like to work with Whitehall Robins on this matter, but that we first need a better understanding of the situation. Whitehall Robins should provide the information which ——— has provided about their CFC testing and what they have agreed and not agreed to do.

A separate supplement should be provided for a different stockpiling site (still need to resolve specifications and tests first): similar issues should be addressed as in S-017, plus full information on the transportation of CFCs from one site to the other (including information about the ——— used for transportation and its preparation to contain CFC propellants).

I asked what was the proposed timeframe for switching stockpiling sites (from ———to ——— ———. He said that it would be "as soon as a supplement is approved for this."

We had asked (in our letter dated March 19, 1998, re: S-017) that a separate supplement be submitted to address CFC blending issues at the manufacturing site for the drug product in ———. They will do this.

He mentioned that a microbiology submission had been sent to us as correspondence.

The following supplements (or supplemental amendments) and target submission times were indicated.

S-020 resubmission: First week in July 1999.

S-017 resubmission: July 1999.

Blending supplement: July 1999.

CFC propellant transfer/new stockpiling site in —: July 1999.

A resubmission to S-— has been submitted earlier this year [——————.

He thanked me for my time. This ended the conversation.

Alan C. Schroeder, Ph.D.

cc: Orig. NDA #16-126 HFD-570/Division file HFD-570/ACSchroeder/6-17-99 HFD-570/GPoochikian HFD-570/CSO PJani	R/D init. by: _____ F/T by: ACSchroeder/6-17-99 ACSfile: N16126-99-06-17.doc ATTACHMENT

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 16-126 / S-020

CORRESPONDENCE

NDA 16-126/S-020

Whitehall-Robins Healthcare
5 Giralda Farms
Madison, New Jersey 07940-0871

Attention: Rich J. Cuprys
Assistant Vice President
Regulatory Affairs

Dear Mr. Cuprys:

Please refer to your supplemental new drug application dated August 22, 1997, received August 25, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Primatene Mist (epinephrine) Inhalation Aerosol.

The user fee goal date for this application is February 25, 1998.

This supplemental application provides for analytical methods, methods validation data and specifications for impurities in each CFC propellant.

We have completed our review and find the information presented is inadequate, and the supplemental application is not approvable under section 505(d) of the Act and 21 CFR 314.125(b). The deficiencies may be summarized as follows:

1.

2.

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16-126/S-020 NOT APPROVABLE LETTER

If you have any questions regarding this supplement, please contact Ms. Parinda Jani, Project Manager, for the Division of Pulmonary Drug Products, at 301-827-1050.

If you have any questions regarding the NDA, please contact Ms. Babette Merritt, Project Manager, for the Division of Over the Counter Drug Products, at (301) 827-2222.

Sincerely yours,

Guirag Poochikian, Ph.D.
Chemistry Team Leader
Division of New Drug Chemistry III
Center for Drug Evaluation and Research

cc:
Original NDA 16-126
HFD-560/Div. files
HFD-820/ONDC Division Director
DISTRICT OFFICE
HFD-92/DDM-DIAB
HFD-570/P.Jani
HFD-570/Schroeder\2-23-98
HFD-570/Poochikian\2-23-98
HFD-570/Schumaker\2-20-98
HFD-560/Merritt
HFD-560/Cook
HFD-830/DD/Dunn

Drafted by:pj /February 9, 1998/
Initialed by:
final: WilsonP\2-24-98

NOT APPROVABLE (NA)