CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 16-126 / S-017

Name:	Primatene Mist Inhalation Aerosol
Sponsor:	Wyeth Consumer Healthcare
Approval Date:	December 1, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 16-126 / S-017

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Administrative Document(s)	X
Correspondence	X

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APPLICATION NUMBER:

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APPROVAL LETTER

NDA 16-126/S-017

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

Attention: Ken Warner
Director
Regulatory Affairs, CMC

Dear Mr. Warner:

Please refer to your supplemental new drug application dated July 24, 1995, received July 25, 1995, 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 May 20, 1996, May 9, and November 25, 1997, and July 30, 1999. Your submission of July 30, 1999, constituted a complete response to our March 19, 1998, action letter.

The supplement provides for stockpiling chlorofluorocarbon (CFC) 12 and 114 propellants at [redacted] for use in Primatene Mist production.

We have completed the review of this supplemental application and it is approved as of the date of this letter. You are reminded that Whitehall-Robins is responsible for full acceptance testing of the CFC propellants, in accordance with the specifications and methods approved in supplement S-020.

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 Parinda Jani, Project Manager, at (301) 827-1064.

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 16-126
HFD-560/DIV. FILES
HFD-570/P.JANI
HFD-570/SCHROEDER/12-1-99
HFD-570/POOCHIKIAN
HFD-570/BARNES/11-30-99
HFD-560/COOK
HFD-560/MERRITT
HFD-830/DUNN
HFD-095/DDMS-IMT
HFD-820/DNDC DIVISION DIRECTOR
DISTRICT OFFICE

DRAFTED BY: PJANI/NOVEMBER 29, 1999
INITIALED BY: SCHROEDER/12-1-99
FINAL:janip/12-1-99
FILENAME: N16126AP.017

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 16-126 / S-017

CHEMISTRY REVIEW(S)

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	SCS-017 7/24/95
8. SUPPLEMENT PROVIDES FOR: stockpiling CFC propellants 12 and 114 for use in drug product manufacture.		9. AMENDMENTS DATES (BC) 5/9/97* (BC) 11/25/97* (*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/3-17-98
HFD-570/GPoochikian
HFD-570/CSO PJani
HFD-570/SJohnson
HFD-560/RCook & BMerritt
R/D Init. by:_____
F/T by: ACSchroeder/3-17-98
doc #N16126_S17.doc

18. CONCLUSIONS AND RECOMMENDATIONS

This is a minor amendment which doesn't address our NA letter dated 1/7/97. This supplement remains Not Approvable until all of the issues in our letter dated 1/7/97 are satisfactorily addressed. PM should prepare a NA letter including deficiencies at end of this review.

19. REVIEWER

NAME	SIGNATURE	DATE COMPLETED
Alan C. Schroeder, Ph.D.		3/17/98

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

Redacted 6 page(s)

of trade secret and/or

confidential commercial

information from

S-017 CHEMISTRY REVIEW 3/17/98

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 16-126 / S-017

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-017

CORRESPONDENCE

NDA 16-126/S-017

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 July 24, 1995, received July 25, 1995, 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 May 20, 1996, and May 9, and November 25, 1997.

The supplement provides for stockpiling chlorofluorocarbons (CFCs) 12 and 114, manufactured and stored by [redacted] for use in Primatene Mist Production.

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 are as follows:

1. [redacted]

2.

3.

4. [redacted]

5. [redacted]

Please submit your response to the above comments and deficiencies in a separate supplement, since a change in manufacturing site has been proposed for the CFC blending operations.

Please respond as soon as possible to the deficiencies listed in our previous letter, dated January 7, 1997, pertaining to supplement S-017. Note that as previously indicated, supplement S-017 may not be approved until supplement S-020 is approved for impurity specifications and tests for CFC propellants. Supplement S-017 remains not approvable until the comments in our letter dated January 7, 1997, are satisfactorily addressed.

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of the options under 21 CFR 314.120 In the absence of such action, FDA may withdraw the application. Any amendment should respond to all the deficiencies listed. A partial reply will not be processed as a major amendment unless it addresses all remaining outstanding deficiencies, nor will the review clock be reactivated until all deficiencies have been addressed.

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

Sincerely yours,

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

APPEARS THIS WAY
ON ORIGINAL

cc:
Original NDA 16-126
HFD-560/Div. files
DISTRICT OFFICE
HFD-570/P.Jani/
HFD-570/SCHUMAKER/3-18-98
HFD-570/SCHROEDER/3-18-98
HFD-570/POOCHIKIAN/3-18-98
HFD-560/COOK
HFD-560/MERRITT
HFD-830/DUNN
DRAFTED BY:PJ/3-18-98
INITIALED BY:SCHROEDERA/3-17-98
FINAL:pj/3—19-98

NOT APPROVABLE