

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 16-126 / S-025

Name: Primatene Mist Inhalation Aerosol

Sponsor: Wyeth Consumer Healthcare

Approval Date: August 30, 2001

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**APPLICATION NUMBER:
NDA 16-126 / S-025**

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APPLICATION NUMBER:
NDA 16-126 / S-025

APPROVAL LETTER



NDA 16-126/S-025

Whitehall-Robins
Attention: Ms. Sharon Heddish
Five Giralda Farms
Madison, NJ 07940-0871

30 AUG 2001

Dear Ms. Heddish:

Please refer to your supplemental new drug application, (NDA) dated March 6, 2000, received on March 7, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Primatene Mist Inhalation Aerosol (epinephrine 5.5 mg/mL).

We acknowledge receipt of your amendments dated June 14, June 21, and November 10, 2000, and July 6, 2001, received March 15, June 23, and November 14, 2000, and July 9, 2001.

The supplemental new drug application provides for:

- (1) revised storage condition specifications statement per approvable letter for S- dated
- (2) addition of a warning statement under the subheading, "When using this product" to alert consumer not to tamper with the container
- (3) conformance with "Drug Facts" labeling in content and format in accordance with 21 CFR 201.66 (c) and (d)

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the draft labeling dated March 6, 2000, with the minor editorial revisions listed below. Accordingly, the application is approved effective on the date of this letter provided that the following changes are made to the labeling:

I. Outer Carton Label for ½ oz. with Mouthpiece, ½ oz. Refill and ¾ oz. Refill:

- A. "Drug Facts" labeling - revise according to the attached prototype.
- B. On all panels, where it reads "Epinephrine Inhalation Aerosol Bronchodilator," relocate the word "Bronchodilator" to a separate line.
- C. For the ¾ fl. oz. Refill:

1. add "Drug Facts (continued)" to the bottom panel.
2. left panel, above "Questions or comments,?" add "Drug Facts (continued)" and a hairline underneath that heading.

II. Consumer information insert:

- A. The title "Drug Facts" can remain as submitted or be removed. If the words "Drug Facts" are used, move the Directions for Use of the Mouthpiece outside the Drug Facts box, move the heavy black line from the right to the middle, extend the hair lines to within 2 spaces of either side of the box, and relocate the "Questions or comments" to an area immediately preceding the Directions for Use of the Mouthpiece. Add "Drug Facts (continued)" if it is necessary to use the second column. The Directions for Use of the Mouthpiece could then remain at the right of the middle line. If the sponsor elects to remove the title "Drug Facts," the Directions for Use of the Mouthpiece can remain anywhere on the Consumer Information Insert.
- B. Same changes be made as on the carton labeling.

III. Container labels for ½ fl. oz. and ¾ fl. oz. sizes - same changes be made as on the carton labeling.

If final printed labeling (FPL) has not been printed, please revise the labeling as indicated above and submit FPL as an amendment to this supplement. If FPL has been printed, please revise the labeling as indicated above at the time of the next printing or within 180 days, whichever comes first, and submit as a new supplement to this application.

The final printed labeling (FPL) must be identical, and include the minor editorial revisions indicated, to the submitted draft labeling (carton and container labels, and Consumer Information Insert submitted March 6, 2000). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. For administrative purposes, this submission should be designated "FPL for approved NDA 16-126." Approval of this submission by FDA is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of the labeling may be required.

NDA 20-463

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If you have any questions, call Babette Merritt, Project Manager, at (301) 827-2222.

Sincerely,

Charles Ganley, M.D.
Director
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Prototype "Drug Facts" Label

Drug facts	
Active ingredient (in each inhalation)	Purpose
Epinephrine 0.22 mg.....	Bronchodilator
Uses	
<ul style="list-style-type: none"> ■ temporarily relieves shortness of breath, tightness of chest, and wheezing due to bronchial asthma ■ eases breathing for asthma patients by reducing spasms of bronchial muscles 	
Warning	
For inhalation only	
Do not use	
<ul style="list-style-type: none"> ■ unless a doctor has said you have asthma ■ if you are now taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric, or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your prescription drug contains an MAOI, ask a doctor or pharmacist before taking this product. 	
Ask a doctor before use if you have	
<ul style="list-style-type: none"> ■ heart disease ■ thyroid disease ■ diabetes ■ high blood pressure ■ ever been hospitalized for asthma ■ trouble urinating due to an enlarged prostate gland 	
When using this product	
<ul style="list-style-type: none"> ■ overuse may cause nervousness, rapid heart beat, and heart problems ■ do not continue to use, but seek medical assistance immediately if symptoms are not relieved within 20 minutes or become worse ■ do not puncture or throw into incinerator. Contents under pressure. ■ do not use or store near open flame or heat above 120°F (49°C). May cause bursting. 	
Contains CFC 12, 114, substances which harm public health and environment by destroying ozone in the upper atmosphere	
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.	
Directions	
<ul style="list-style-type: none"> ■ do not use more often or at higher doses unless directed by a doctor ■ supervise children using this product ■ adults and children 4 years and over: start with one inhalation, then wait at least 1 minute. If not relieved, use once more. Do not use again for at least 3 hours. ■ Children under 4 years: ask a doctor 	
Other information	
<ul style="list-style-type: none"> ■ store at room temperature, between 20-25°C (68-77°F) ■ see insert for mouthpiece use and care instructions 	
Inactive ingredients alcohol 34%, ascorbic acid, fluorocarbons (propellant), water	
Questions or comments? Call 1-8 PRIMATENE or 1-877-462-8363 weekdays 9 AM-5 PM EST www.Primatene.com	

The prototype label shown above should be followed in content only. The font sizes for title, headings, subheadings, condensed text and other graphic features are required to be in accordance with provisions of 21 CFR 201.66.

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

/s/

Charles Ganley

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 16-126 / S-025

LABELING REVIEW(S)

PRIMATENE[®] MIST INHALANT

NDA Labeling Review

NDA 16-126 (SLR-025)

Submission Date: March 6, 2000
March 14, 2000
June 21, 2000
April 16, 2001
July 6, 2001

Review Date: July 17, 2000
August 29, 2000
September 18, 2000
August 6, 2001

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

**Applicant's
Representative:** David S. Smith, Ph.D.
Director, Regulatory Affairs
973-660-6806

Drug: Primatene Mist Inhalation Aerosol
Epinephrine 5.5 mg/mL

**Pharmacologic
Category:** Bronchodilator

Submitted: Carton Label with mouthpiece for ½ oz.
Aerosol Container Labels for ½ oz. and ¾ oz.
Refill Carton Labels for ½ oz. and ¾ oz.
Consumer Information Insert

Background: The sponsor submitted a supplement for changes in labeling being effected in 30 days. The changes include (1) a different storage condition from 15°C-30°C (59°F-86°F) to 15°C-25°C (59°F-77°F) in accordance with the agency's request in an approvable letter dated February 27, 1998, (2) the addition of a warning statement under the subheading "When using this product" alerting the consumer not to tamper with the container, in accordance with 21 CFR 314.70(c)(2)(i), and (3) conformance with Drug Facts content and format.

**Reviewer's
Comments:** A review of labeling in this submission uses a single strikeout to indicate the Agency's recommendation for deletion, and shading indicates addition. The sponsor's specifications for Drug Facts meet 21 CFR 201.66 format requirements.

PRIMATENE[®] MIST INHALANT

1. Carton Label

- ½ fl. oz. with mouthpiece
- ½ fl. oz. refill
- ¾ fl. oz. refill

I Principal Display Panels

A. Statement of Identity

The pharmacologic category or purpose (bronchodilator) was in a line separate from the active ingredient (epinephrine) and dosage form (inhalation aerosol) in prior approved labeling. The same format should be used in the currently submitted labeling.

II. Drug Facts Panel(s)

- A. The ½ oz. container carton with mouthpiece has one panel only and is shown immediately below with reviewer's comments which apply to Drug Facts panels on Cartons for all units. The ½ oz. and ¾ oz. refill cartons contain the same Drug Facts on 4 panels with some format differences to be discussed further below.

Drug Facts	
Active ingredient (in each inhalation)	Purpose
Epinephrine 0.22 mg.....	Bronchodilator
Uses	
<ul style="list-style-type: none"> ■ temporarily relieves shortness of breath, tightness of chest, and wheezing due to bronchial asthma ■ eases breathing for asthma patients by reducing spasms of bronchial muscles 	
Warnings	
<p style="text-align: center;">Reviewer's comment: no flammability warning needed. Sponsor tested 3 lots per 16 CFR 1500.45 for flammability per actuation. Results indicate that product is not flammable per Agency chemist.</p>	
For inhalation only	
Do not use	
<ul style="list-style-type: none"> ■ unless a _____ doctor has said you have asthma <p style="text-align: center;">Reviewer's comment: more consumer friendly language</p> <ul style="list-style-type: none"> ■ if you are now taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric, or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your prescription drug contains an MAOI, ask a doctor or pharmacist before taking this product. 	
Ask a doctor before use if you have	
<ul style="list-style-type: none"> ■ heart disease ■ thyroid disease ■ diabetes ■ high blood pressure ■ ever been hospitalized for asthma ■ trouble urinating due to an enlarged prostate gland 	
When using this product	
<ul style="list-style-type: none"> ■ _____ <p style="text-align: center;">Reviewer's comment: is part of Directions below</p> <ul style="list-style-type: none"> ■ _____ overuse may cause nervousness, _____ rapid heart beat, and, _____ heart problems <p style="text-align: center;">Reviewer's comment: more consumer friendly language</p> <ul style="list-style-type: none"> ■ do not continue to use, but seek medical assistance immediately if symptoms are not relieved within 20 minutes or become worse 	

PRIMATENE[®] MIST INHALANT

<p>do not puncture or throw into incinerator. Contents under pressure. Reviewer's comment: more consumer friendly language</p> <p>do not use or store near open flame or heat — above 120°F (49°C). May cause bursting. Reviewer's comment: more consumer friendly language</p>
<p>Contains CFC 12, 114, substances which harm public health and environment by destroying ozone in the upper atmosphere</p> <p>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.</p>
<p>Directions</p> <p>do not use more often or at higher doses unless directed by a doctor</p> <p>supervise children using this product</p> <p>adults and children 4 years and over start with one inhalation, then wait at least 1 minute. If not relieved, use once more. Do not use again for at least 3 hours.</p> <p>children under 4 years ask a doctor Reviewer's comment: more consumer friendly language</p> <p>see insert for mouthpiece use and care instructions Reviewer's comment: relocated to Other information</p>
<p>Other information</p> <p>store at room temperature, between 15-25°C (59-77°F) Reviewer's comment: USP specifications</p> <p>see insert for mouthpiece use and care instructions Reviewer's comment: relocated from Directions</p> <p>Reviewer's comment: inactive ingredients reveal same information</p>
<p>Inactive ingredients alcohol 34%, ascorbic acid, fluorocarbons (propellant), water</p>
<p>Questions or comments? Call 1-8 PRIMATENE or 1-877-462-8363 weekdays 9 AM-5 PM EST at 1-8 PRIMATENE or 1-877-462-8363 www.Primatene.com Reviewer's comment: the telephone number should follow "Questions" per 21 CFR 201.66(c)(9) and the "or" next to the number should be unbolded</p>

B. In the ¼ oz. container refill, the bottom panel needs the addition of "Drug Facts (continued)" per 21 CFR 201.66(c)(1).

III. Other panels

A. top, bottom, left side and right side of ½ oz. container with mouthpiece, top panel of ¼ oz. refill.
The word "bronchodilator" should be placed on another line for reasons explained under the Principal Display Panel(s) above

B. Top panel of ½ oz. container with mouthpiece
bottom panel of ½ oz. refill
top panel of ¼ oz. refill

Uses the phrase "Tamper-Evident Aerosol Container." The last approved labeling used the phrase "Tamper-Resistant Aerosol Container." The change is acceptable per 21 CFR 211.132.

2. Container Label

The same changes on the Carton label should be made to the container label.

PRIMATENE[®] MIST INHALANT

3. Consumer Information Insert

- A. If the title "Drug Facts" remains, it is appropriate to use the content and format as described in 21 CFR 201.66 and to enter the same changes as in the Carton label. Therefore, the Directions for Use of the Mouthpiece should be placed outside the Drug Facts box. The Directions for Use of the Mouthpiece could be put to the right of the Drug Facts box. If the second column is used, the title "Drug Facts (continued)" would need to be used. If the words "Drug Facts" are removed, the Directions for Use of the Mouthpiece can remain anywhere on the Consumer Information Insert.
- B. The section entitled "Directions for Use of Mouthpiece" in the currently marketed product differs from that in the proposed labeling. The current labeling says "Place other end of mouthpiece on bottle," and "Replace plastic cap on mouthpiece." The proposed labeling says respectively "Place short end of mouthpiece on bottle" and "For storage, place long end of mouthpiece back on bottle and cover with plastic cap." These changes are acceptable.
- C. The section entitled "Care of the Mouthpiece" in the currently marketed product differs from the proposed labeling by saying "The Primatene Mist mouthpiece should be washed once daily with soap and hot water, and rinsed thoroughly. Then it should be dried with a clean, lint free cloth." The proposed labeling says "The Primatene Mist mouthpiece should be washed after each use with hot, soapy water, rinsed thoroughly, and dried with a clean, lint-free cloth." This change is acceptable.

Reviewer's Recommendation:

- A. The following information should be relayed to the Sponsor:
- I. **Outer Carton Label for Mouthpiece package and Aerosol Containers of ½ oz. and ¾ oz.:**

DRUG FACTS

- A. Under Warnings
1. A flammability warning is not needed.
 2. Do not use:
 - a. Change the 1st bullet from "_____ " to "unless a doctor has said you have asthma."
 3. When using this product:
 - a. Delete the 1st bullet "_____ "
 - b. Change the 2d bullet from "_____ " to "overuse may cause nervousness, rapid heart beat, and heart problems."

PRIMATENE[®] MIST INHALANT

- c. Change the 4th bullet from "~~_____~~" to "do not puncture or incinerate. Contents under pressure."
- d. Change the 5th bullet from "~~_____~~" to "do not use or store near open flame or heat above 49°C (120°F). May cause bursting."

B. Under Directions

1. Add "do not use more often or at higher doses than recommended unless directed by a doctor" as the first bullet.
2. Change the 2d bullet from "~~_____~~" to "supervise children using this product."
3. Change the 3rd bullet, 1st phrase, from "~~_____~~" to "adults and children 4 years and over, start with one inhalation, then wait at least 1 minute."
4. Change the 4th bullet from "~~_____~~" to "children under 4 years: ask a doctor."

C. Under Other information

1. Change the 1st bullet temperature range from "15-25°C (59-77°F)" to "20-25°C (68-77°F)."
2. Delete the 3d bullet "~~_____~~."

D. Under Questions or comments

1. Debold the word "or" that precedes the telephone number.
2. Relocate the telephone number to precede the day and time phrase (i.e., 1-8- PRIMATENE or 1-877-462-8363 weekdays 9AM-5PM EST).

E. For the ¾ fl. oz. refill, add "Drug Facts (continued)" to the bottom panel.

F. On panels of all cartons, where it reads "Epinephrine Inhalation Aerosol Bronchodilator," relocate the word "Bronchodilator" to a separate line.

G. On ¾ oz. refill carton, left panel, above "Questions or comments,?" add "Drug Facts (continued)" and a hairline underneath that heading.

**APPEARS THIS WAY
ON ORIGINAL**

II. Consumer information insert:

- A. The title "Drug Facts" can remain as submitted or be removed. If the words "Drug Facts" are used, move the Directions for Use of the Mouthpiece outside the Drug Facts box, move the heavy black line from the right to the middle, extend the hair lines to within 2 spaces of

PRIMATENE[®] MIST INHALANT

either side of the box, and relocate the "Questions or comments" to an area immediately preceding the Directions for Use of the Mouthpiece. Add "Drug Facts (continued)" if it is necessary to use the second column. The Directions for Use of the Mouthpiece could then remain at the right of the middle line. If the sponsor elects to remove the title "Drug Facts," the Directions for Use of the Mouthpiece can remain anywhere on the Consumer Information Insert.

B. It is recommended that the same changes be made as on the carton labeling.

III. Container labels for ½ fl. oz. and ¾ fl. oz. sizes:

A. It is recommended that the same changes be made as on the carton labeling.

IV. An Approved letter should be sent to the sponsor for the labeling submitted with this supplement. Inform the sponsor, if it has not printed final printed labeling (FPL), it should revise the labeling as indicated above and submit FPL as an amendment to this supplement. If FPL has been printed, request sponsor to revise the labeling as indicated above at the time of next printing or within 180 days, whichever comes first, and submit as a new supplement to this application.

V. Provide the sponsor with the attached "Drug Facts" prototype label as a guideline.

Michael T. Benson, R.Ph., J.D. Regulatory Review Pharmacist	Marina Chang, R.Ph. Leader, Team 1
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Attachment: prototype Drug Facts labeling

Prototype "Drug Facts" Label

PRIMATENE[®] MIST INHALANT

Drug facts	
Active ingredient (in each inhalation)	Purpose
Epinephrine 0.22 g.....	Bronchodilator
Uses	
<ul style="list-style-type: none"> ■ temporarily relieves shortness of breath, tightness of chest, and wheezing due to bronchial asthma ■ eases breathing for asthma patients by reducing spasms of bronchial muscles 	
Warning	
For inhalation only	
Do not use	
<ul style="list-style-type: none"> ■ unless a doctor has said you have asthma ■ if you are now taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric, or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your prescription drug contains an MAOI, ask a doctor or pharmacist before taking this product. 	
Ask a doctor before use if you have	
<ul style="list-style-type: none"> ■ heart disease ■ thyroid disease ■ diabetes ■ high blood pressure ■ ever been hospitalized for asthma ■ trouble urinating due to an enlarged prostate gland 	
When using this product	
<ul style="list-style-type: none"> ■ overuse may cause nervousness, rapid heart beat, and heart problems ■ do not continue to use, but seek medical assistance immediately if symptoms are not relieved within 20 minutes or become worse ■ do not puncture or throw into incinerator. Contents under pressure. ■ do not use or store near open flame or heat above 120°F (49°C). May cause bursting. 	
Contains CFC 12, 114, substances which harm public health and environment by destroying ozone in the upper atmosphere	
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.	
Directions	
<ul style="list-style-type: none"> ■ do not use more often or at higher doses unless directed by a doctor ■ supervise children using this product ■ adults and children 4 years and over: start with one inhalation, then wait at least 1 minute. If not relieved, use once more. Do not use again for at least 3 hours. ■ Children under 4 years: ask a doctor 	
Other information	
<ul style="list-style-type: none"> ■ store at room temperature, between 20-25°C (68-77°F) ■ see insert for mouthpiece use and care instructions 	
Inactive ingredients alcohol 34%, ascorbic acid, fluorocarbons (propellant), water	
Questions or comments? Call 1- 8 PRIMATENE or 1-877-462-8363 weekdays 9 AM-5 PM EST www.Primatene.com	

The prototype label shown above should be followed in content only. The font sizes for title, headings, subheadings, condensed text and other graphic features are required to be in accordance with provisions of 21 CFR 201.66.

PRIMATENE[®] MIST INHALANT

cc: NDA 16-126
HFD-560: Division File
HFD-560: CGanley/LKatz
HFD-560: Benson/MChang/Merritt
R/D: MBenson 8/06/01

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/s/

Michael Benson
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Charles Ganley
9/7/01 06:19:17 PM
MEDICAL OFFICER

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 16-126 / S-025

ADMINISTRATIVE DOCUMENTS

MEMORANDUM OF TELEPHONE CONVERSATION

Date: November 26, 2001

BETWEEN: Loren Quinn
Whitehall Robins
973-660-6167

and Marina Chang, Leader, Team #1
Michael T. Benson, Regulatory Review Pharmacist (HFD-560)

Subject: Primatene Mist NDA 16-126; S-25

We called Ms. Quinn to verify that the sponsor will include in the Drug Facts label of Primatene Mist the statement "Ask a doctor or pharmacist before use if you are taking any prescription drug for asthma." Ms. Quinn said the sponsor is aware of the need to include that statement on the label as advised by Mr. Benson in a telephone conversation on September 24, 2001. A prototype of the updated label is attached.

Marina Chang, R.Ph.

Michael T. Benson, J.D., R.Ph.

Attachment

Prototype "Drug Facts" Label

Drug facts	
Active ingredient (in each inhalation)	Purpose
Epinephrine 0.22 mg.....	Bronchodilator
Uses	
<ul style="list-style-type: none"> ■ temporarily relieves shortness of breath, tightness of chest, and wheezing due to bronchial asthma ■ eases breathing for asthma patients by reducing spasms of bronchial muscles 	
Warning	
For inhalation only	
Do not use	
<ul style="list-style-type: none"> ■ unless a doctor has said you have asthma ■ if you are now taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric, or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your prescription drug contains an MAOI, ask a doctor or pharmacist before taking this product. 	
Ask a doctor before use if you have	
<ul style="list-style-type: none"> ■ heart disease ■ thyroid disease ■ diabetes ■ high blood pressure ■ ever been hospitalized for asthma ■ trouble urinating due to an enlarged prostate gland 	
Ask a doctor or pharmacist before use if you are taking any prescription drug for asthma.	
When using this product	
<ul style="list-style-type: none"> ■ overuse may cause nervousness, rapid heart beat, and heart problems ■ do not continue to use, but seek medical assistance immediately if symptoms are not relieved within 20 minutes or become worse ■ do not puncture or throw into incinerator. Contents under pressure. ■ <u>do not use or store near open flame or heat above 120°F (49°C). May cause bursting.</u> 	
Contains CFC 12, 114, substances which harm public health and environment by destroying ozone in the upper atmosphere	
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.	
Directions	
<ul style="list-style-type: none"> ■ do not use more often or at higher doses unless directed by a doctor ■ supervise children using this product ■ adults and children 4 years and over: start with one inhalation, then wait at least 1 minute. If not relieved, use once more. Do not use again for at least 3 hours. ■ Children under 4 years: ask a doctor 	
Other information	
<ul style="list-style-type: none"> ■ store at room temperature, between 20-25°C (68-77°F) ■ see insert for mouthpiece use and care instructions 	
Inactive ingredients alcohol 34%, ascorbic acid, fluorocarbons (propellant), water	
Questions or comments? Call 1- 8 PRIMATENE or 1-877-462-8363 weekdays 9 AM-5 PM EST www.Primatene.com	

The prototype label shown above should be followed **in content only**. The font sizes for title, headings, subheadings, condensed text and other graphic features are required to be in accordance with provisions of 21 CFR 201.66.

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/s/

Michael Benson
1/22/02 03:22:24 PM
INTERDISCIPLINARY

MEMORANDUM OF TELEPHONE CONVERSATION

Date: September 24, 2001

BETWEEN: Loren Quinn
Whitehall Robins
973-660-6167

and Michael T. Benson (HFD-560)

Subject: Primatene Mist NDA 16-126; S-25

Babette Merritt left me a message saying that Loren Quinn called and asked about the temperature storage conditions for Primatene Mist on the prototype "Drug Facts" label sent to Whitehall Robins on or about August 30, 2001.

I called Ms. Quinn and advised her that the temperature numbers were changed from those originally indicated by the sponsor to be consistent with the USP Temperature Storage Statement. Ms. Quinn asked why the statement "Ask a doctor or pharmacist before use if you are taking any prescription drug for asthma." was not included in the prototype label. I checked an earlier draft labeling review and found that the statement was pushed outside of the table created in the sponsor's diskette and blinded from being shown in the table in Microsoft Word. The blinding was not noticed until the time of this telephone call. I explained to her why the statement was not included and advised her to include that statement in the Drug Facts label. She thanked me and our conversation concluded cordially.

Michael T. Benson, J.D., R.Ph.

MEMORANDUM OF TELEPHONE CONVERSATION

Date: May 17, 2001

BETWEEN: David S. Smith, Ph.D.
Director, Regulatory Affairs
Whitehall Robins
973-660-6806

and Michael T. Benson, R.Ph., J.D.
Walter Ellenberg, Ph.D.

Subject: Flash Point of Primatene® Mist Inhalation Aerosol, NDA 16-126

Background:

Whitehall Robins had submitted amendment S-025 which stated that flashpoint data were enclosed, but the data were missing. On April 16, 2001, Michael Benson and Babette Merritt called Dr. Smith to request the missing data. By letter dated April 16th, Dr. Smith submitted the missing data which indicated that flammability testing was done on the solution inside the container. What the Agency seeks is flammability testing on the contents sprayed to determine the flash point.

Telephone Conversation:

The Agency explained to Dr. Smith the problem encountered with the flammability testing as described above and what needs to be done to properly address the issue. Dr. Smith said he would contact his company's department that handles this type of testing. He did not know how long it would take to complete the study and is to call back with an expected completion date.

The conversation concluded cordially.

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/s/

Michael Benson
5/23/01 09:54:52 AM
INTERDISCIPLINARY

Walter J. Ellenberg
6/8/01 03:29:02 PM
CSO

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICES
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: May 9, 2001
FROM: Charlotte Yaciw, Chemist, HFD-830/550
THROUGH: John Smith, Team Leader, HFD-550
TO: NDA 16-126
SUBJECT: SLR*-025/BC dated April 16, 2001, received April 27, 2001

The information presented in this submission does not address the question "Is there a flammability risk to the user?" since no testing was performed on the spray plume delivered when the MDI is actuated by the user.

Primatene Mist Inhalation Aerosol is a hydro-alcoholic solution of epinephrine with — 12 and 114 as propellants. The ethanol content is 34%. This high level has raised the concern that the aerosol could flash if activated near a flame. The referenced amendment contains a report on the flammability of the product. The data were generated using the method in ASTM D 56-98a which measures the flammability of the solution itself, i.e., open the container and decant the contents for testing. The product was found not flammable due to the presence of the — carriers, however, the applicability of the result is questionable since it does not simulate the actual use of the product by the consumer, i.e., the flammability (or lack thereof) of the spray plume.

This review was done at the request of the OTC labeling reviewer, M. Benson.

*The jacket reviewed was miscoded SCM instead of SLR.

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/s/

Charlotte Yaciw
5/11/01 01:28:31 PM
CHEMIST
HFD-560 will make the final decision on this supplement.

John Smith
5/14/01 07:27:35 AM
CHEMIST