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APPROVAL PACKAGE FOR:

APPLICATION NUMBER

20-949

Chemistry Review(s)

DIVISION OF PULMONARY & ALLERGY DRUG PRODUCTS

Chemist NDA Review

REVIEW OF CHEMISTRY MANUFACTURING & CONTROLS

NDA No.: N 20949
CHEM. REVIEW: # 3

REVIEW COMPLETION DATE: April 26, 2001
REVIEWER: Vibhakar Shah, Ph.D.

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE	COMMENT
Amendment (AZ)*	October 27, 2000	October 30, 2000	October 31, 2000	Response to 6-06-2000 AE letter
Amendment (BC)*	December 12, 2000	December 14, 2000	December 18, 2000	Withdrawal of DMFs
Amendment (BC)*	February 27, 2001	March 01, 2001	March 06, 2001	CMC information
Amendment (BL)*	March 07, 2001	March 09, 2001	March 14, 2001	Labeling
Amendment (BC)*	March 12, 2001	March 13, 2001	March 15, 2001	Stability data
Amendment (BC)*	March 30, 2001	April 02, 2001	April 04, 2001	Response to 3-16-2001 fax comments
Amendment (BC)*	April 11, 2001	April 12, 2001	April 13, 2001	Methods Validation Package
Amendment (BC)*	April 17, 2001	April 18, 2001	April 19, 2001	Revised MVP
Amendment (BL)*	April 17, 2001	April 18, 2001	April 19, 2001	Labeling
Amendment (BL)*	April 20, 2001	April 23, 2001	April 24, 2001	Revised Labeling
Amendment (BL)*	April 25, 2001	April 25, 2001	April 26, 2001	Revised Labeling
Amendment (BC)	May 19, 2000	May 24, 2000	May 31, 2000	Refer to
Amendment (BC)	May 05, 2000	May 05, 2000	May 12, 2000	Chem. Rev. 2
Amendment (BC)	January 20, 2000	January 21, 2000	January 28, 2000	February 26, 1999
Amendment (AZ)	December 03, 1999	December 06, 1999	December 09, 1999	
Amendment (BZ)	July 17, 1998	July 20, 1998	July 20, 1998	
Amendment (BC)	July 01, 1998	July 06, 1998	July 09, 1998	Refer to
Amendment (BZ)	June 19, 1998	June 24, 1998	June 29, 1998	Chem. Rev. 1
Amendment (BZ)	June 09, 1998	June 10, 1998	June 16, 1998	February 26, 1999
Amendment (BZ)	May 18, 1998	May 19, 1998	May 28, 1998	
Correspondence	May 04, 1998	May 08, 1998	May 12, 1998	
Original Submission	March 27, 1998	March 30, 1998	April 08, 1998	6 CMC Volumes

* Subjects of this review

NAME & ADDRESS OF APPLICANT:

Dey Laboratories
2751 Napa Valley Corporate Drive
Napa, CA 94558
Tel: (707) 224-3200
Fax: (707) 224-3235

DRUG PRODUCT NAME:

Proprietary: AccuNeb™ (Albuterol sulfate) Inhalation Solution.
Nonproprietary/USAN: Albuterol sulfate Inhalation Solution
Code Name/#: Not applicable
Chemical Type/Therapeutic Class: 5 S

PHARMACOLOGICAL CATEGORY:

Indication:
Dosage Form: Inhalation Solution
Strengths: 1.5 mg Albuterol sulfate/3 mL (equiv. to 1.25 mg albuterol/3mL)
0.75 mg Albuterol sulfate/3mL (equiv. to 0.63 mg albuterol/3 mL)

Maximum Daily Dose: 3 - 4 vials/day, i.e., TDI = 2.5 - 5 mg
Route of Administration: Oral-Inhalation through Nebulization
Dispensed as: Rx OTC

SPECIAL PRODUCTS: Yes No

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: 1,3-benzenedimethanol, α^1 -[[[1,1-dimethylethyl]amino]-methyl]-4-hydroxy-, sulfate (2:1) salt, or α^1 -[tert-butylamino)methyl]-4-hydroxy-m-xylene- α,α' -diol sulfate (2:1) salt

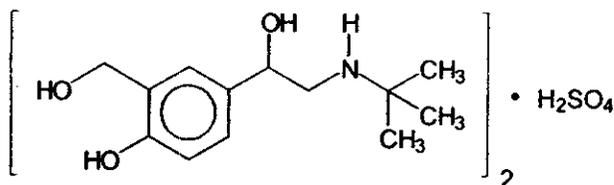
Molecular Formula: $(C_{13}H_{21}NO_3)_2 \cdot H_2SO_4$

Molecular Weight: 576.71

CAS Registry No: [51022-70-9]

Molecular Formula (Base): $C_{13}H_{21}NO_3$

Molecular Weight: 239.31



Albuterol sulfate (USP 23, p 39)

SUPPORTING DOCUMENTS:

A. DMFs:

DMF/Type	DMF Holder	Subject	LOA Date	Status	Reference/Comment
DMF [redacted] Type II		Mfg. of Albuterol sulfate, USP	01-10-1997	Adequate	Refer to CR #2, 06-02-2000
DMF [redacted] Type III			05-12-1997	Adequate	Refer to CR #4, 03-19-2001 IR letter issued, 03-20-2001
DMF [redacted] Type III			07-26-2000	Adequate	DMF CR #3, 02-04 2000, Liu, S.H./HFD-623; DMF CR #2, 03-25-1999, V.Shah/HFD-820, Refer to p. 35 of this Review
DMF [redacted]			3-05-1999	Adequate	DMF CR #1, 03-20-2001 In support of DMF [redacted] Refer to p 35 of this review.
DMF [redacted]			03-05-1999	Adequate	DMF CR #1, 03-20-2001 In support of DMF [redacted] Refer to p 35 of this review.
DMF [redacted]			03-10-1999	Adequate	DMF CR #1, 03-21-2001 In support of DMF [redacted] Refer to p 35 of this review.
DMF [redacted] Type III				Withdrawn	Discontinued as an [redacted] for the drug product. Refer to p. 34 of this Review
DMF [redacted]			07-06-1999		
DMF [redacted]			07-06-1999	Withdrawn	Secondary DMFs which were referenced in support of DMF [redacted]
DMF [redacted]			07-08-1999		
DMF [redacted] Type III			12-12-2000	Withdrawn	Amendment 12-12-2000
DMF [redacted] Type III			12-12-2000	Withdrawn	Amendment 12-12-2000

Date Format: MM-DD-YYYY

B. INDs/NDAs:

The following Investigational New Drug Application (IND) has been specified by the applicant in support of this application.

IND 44281 Albuterol sulfate Inhalation solution.

RELATED DOCUMENTS (if applicable): Numerous NDAs and ANDAs

There are numerous approved NDAs and ANDAs for albuterol as an API in Inhalation Solutions, MDIs, DPIs, Aerosols, Tablets and syrups. The following list identifies the NDAs that have been approved in the Division of Pulmonary drug products (HFD-570) for albuterol as an API in the drug products.

<u>NDA #</u>	<u>Status</u>	<u>Date</u>	<u>CT</u>	<u>Sponsor</u>	<u>Drug Name</u>
N017559	AP	01-May-1981	1	Schering	Proventil (Albuterol) Mdi
N017853	AP	07-May-1982	3	Schering	Proventil Tablets
N018062	AP	19-Jan-1983	3	Schering	Proventil (Albuterol) Syrup
N018473	AP	01-May-1981	5	Glaxo Wellcome	Ventolin (Albuterol) MDI
N019112	AP	10-Jul-1986	5	Glaxo Wellcome	Ventolin Tab (Albuterol)
N019243	AP	14-Jan-1987	3	Schering	Proventil (Albuterol) Inhalation Solution
N019269	AP	16-Jan-1987	5	Glaxo Wellcome	Ventolin (Albuterol Sulfate) Sol Inhalation
N019383	AP	13-Jul-1987	3	Schering	Proventil (Albuterol Sulfate) Repetabs
N019489	AP	04-May-1988	3	Glaxo Wellcome	Ventolin Rotacaps Inhalation (Albuterol S04)
N019604	AP	23-Dec-1992	3	Muro Pharm	Volmax (Albuterol S04) Tablets Oros
N019621	AP	10-Jun-1987	5	Glaxo Wellcome	Ventolin Syrup (Albuterol Sulfate)
N019773	AP	23-Apr-1992	3	Glaxo Wellcome	Ventolin
N020291	AP	24-Oct-1996	4	Boehringer Ingelheim	Combivent (Albuterol Sulfate)
N020503	AP	15-Aug-1996	3	3m Pharmaceuticals	Proventil-HFA Inhalation Aerosol

CONSULTS:

<u>Consult</u>	<u>Forward Date</u>	<u>Status</u>	<u>Comments</u>
1. Establishment Evaluation (EER)	01-23-2001	Acceptable 02-01-2001	Refer to p 60 of this review.
2. Microbiology (HFD-160)	01-20-2000	Approval 05-10-2000	Refer to CR #2, 06-02-2000
3. Pharmacology (HFD-570)	01-25-2001	Acceptable 02-22-2001	Consult to evaluate proposed specification for _____ in the drug product Refer to p 25 of this review.
4. Biometrics	-	-	Not needed based upon the updated stability data. Refer to p 51 of this review.
5. Methods Validation		Pending	See p 57, and p 67 of this review.
6. Labeling & Nomenclature (OPDRA/HFD-400)	01-11-2000	Acceptable 04-27-2000	Refer to CR #2, 06-02-2000 and section VI/pages 57, 68-69 and 98 of this review.
7. Environmental Assessment	04-14-2000	Acceptable 05-18-2000	Refer to p 105 of CR #2, 06-02-2000

CR = Chemist Review; Date format: MM-DD-YYYY

REMARKS/COMMENTS: See attached Review Notes

- From GMP perspective, all the establishments that are involved in the manufacture and testing of this drug product have been found acceptable by the Office of Compliance (see EERS report dated February 01, 2001).
- Methods validation package has been submitted and is pending evaluation from the FDA laboratories (see p 57 and p 67 of this review).
- Applicant has agreed to provide mock-up samples of the container-closure system (C with label, carton) prior to launching the drug product for marketing. 1

CONCLUSIONS & RECOMMENDATIONS:

From CMC viewpoint, NDA 20949 for AccuNeb™ (albuterol sulfate) Inhalation Solution, submitted by Dey Laboratories may be approved. The commitments and agreements listed on page 70 of this review should be communicated to the applicant in an appropriate action letter.

15

Vibhakar J. Shah, Ph.D.
Review Chemist, DNDCII (HFD-820)

cc:

<input checked="" type="checkbox"/> Org. NDA 20949	<input checked="" type="checkbox"/> HFD-570/Chemist/VShah	<input checked="" type="checkbox"/> HFD-570/TL/Gpoochikian	
<input checked="" type="checkbox"/> HFD-570/Division File	<input checked="" type="checkbox"/> HFD-570/CSO/DHilfiker		

R/D Init by: GPoochikian/

Document: n20949CMCRev3.doc (Total pages = 110)

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and/or confidential

commercial information

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this page is the manifestation of the electronic signature.**

/s/

Vibhakar J. Shah
4/27/01 03:18:28 PM
CHEMIST

From CMC viewpoint, NDA 20949 for AccuNeb [albuterol sulfate] Inhalati
on Solution by Dey, L. P. may be approved. The commitments and/or ag
reements listed in this review should be communicated to Dey in an app
ropriate action letter.

Guiragos Poochikian
4/27/01 05:43:51 PM
CHEMIST

H. Hiker

JUN - 2 2000

Chemist NDA Review
REVIEW OF CHEMISTRY MANUFACTURING & CONTROLS

NDA No.: N 20949
CHEM. REVIEW: # 2

REVIEW COMPLETION DATE: May 31, 2000
REVIEWER: Vibhakar Shah, Ph.D.

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE	COMMENT
Amendment (AZ)*	December 03, 1999	December 06, 1999	December 09, 1999	*Subjects of this review
Amendment (BC)*	January 20, 2000	January 21, 2000	January 28, 2000	
Amendment (BC)*	May 05, 2000	May 05, 2000	May 12, 2000	
Amendment (BC)*	May 19, 2000	May 24, 2000	May 31, 2000	Refer to Chem. Rev. 1 February 26, 1999
Amendment (BZ)	July 17, 1998	July 20, 1998	July 20, 1998	
Amendment (BC)	July 01, 1998	July 06, 1998	July 09, 1998	
Amendment (BZ)	June 19, 1998	June 24, 1998	June 29, 1998	
Amendment (BZ)	June 09, 1998	June 10, 1998	June 16, 1998	
Amendment (BZ)	May 18, 1998	May 19, 1998	May 28, 1998	
Correspondence	May 04, 1998	May 08, 1998	May 12, 1998	
Original Submission	March 27, 1998	March 30, 1998	April 08, 1998	6 CMC Volumes

NAME & ADDRESS OF APPLICANT:

Dey Laboratories
2751 Napa Valley Corporate Drive
Napa, CA 94558
Tel: (707) 224-3200
Fax: (707) 224-3235

DRUG PRODUCT NAME:

Proprietary: AccuNeb™ (Albuterol sulfate) Inhalation Solution.
Nonproprietary/USAN: Albuterol sulfate Inhalation Solution
Code Name/#: Not applicable
Chemical Type/Therapeutic Class: 5 S

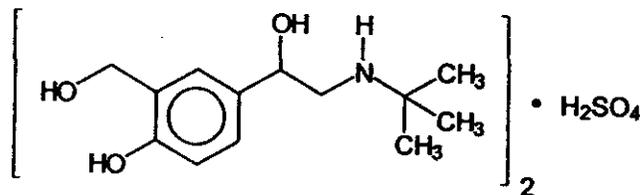
PHARMACOLOGICAL CATEGORY:

INDICATION: []
DOSAGE FORM: []
STRENGTHS: 0.042% (1.25 mg/3 mL), 0.021 % (0.63 mg/3 mL)
Maximum Daily Dose: 3 - 4x /day, i.e., TDI = 2.5 - 5 mg
ROUTE OF ADMINISTRATION: Oral-Inhalation through Nebulization
DISPENSED AS: Rx OTC
SPECIAL PRODUCTS: Yes No

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: 1,3-benzenedimethanol, α^1 -[[[(1,1-dimethylethyl)amino]-methyl]-4-hydroxy-, sulfate (2:1) salt, or α^1 -[tert-butylamino)methyl]-4-hydroxy-m-xylene- α, α' -diol sulfate (2:1) salt

Molecular Formula: $(C_{13}H_{21}NO_3)_2 \cdot H_2SO_4$
Molecular Weight: 576.71
CAS Registry No: [51022-70-9]



Albuterol sulfate (USP 23, p 39)

SUPPORTING DOCUMENTS:

A. DMFs:

DMF/Type	DMF Holder	Subject	LOA Date	Status	Reference
DMF Type II	/	Mfg. of Albuterol sulfate, USP	01-10-1997	Adequate	DMF Review 14, 05-30-2000, V.Shah/HFD-820, Refer to p. 6 of this Review
DMF Type III	/	/	05-12-1997	Adequate IR Letter sent	DMF Review 3, 05-30-2000 V. Shah/HFD-820, Refer to p. 50 of this Review
DMF Type III	/	/	08-27-1999	Inadequate Def. Letter sent	DMF Review 1, 05-31-2000 V. Shah/HFD-820, Refer to p. 91 of this Review
DMF	/	/	07-06-1999	Adequate IR Letter sent	DMF Review 1, 05-30-2000 V. Shah/HFD-820
DMF	/	/	07-06-1999	Adequate IR Letter sent	DMF Review 1, 05-30-2000 V. Shah/HFD-820
DMF	/	/	07-08-1999	Adequate	DMF Review 1, 05-30-2000 V. Shah/HFD-820
DMF Type III	/	/	05-21-1998	Inadequate Def. Letter sent	DMF Review #2, 05-31-2000, V.Shah/HFD-820, Refer to p. 66, 68 of this Review
DMF Type III	/	/		Inadequate Def. Letter sent	DMF Review 1, 05-30-2000 V. Shah/HFD-820, Refer to p. 72 of this Review

B. INDs/NDAs:

The following IND has been specified by the applicant in support of this application.

IND 44281 Albuterol sulfate Inhalation solution.

RELATED DOCUMENTS (if applicable): Numerous NDAs and ANDAs

There are numerous approved NDAs and ANDAs for albuterol as an API in Inhalation Solutions, MDIs, DPIs, Aerosols, Tablets and syrups. The following list identifies the NDAs that have been approved in the Division of Pulmonary drug products (HFD-570) for albuterol as an API in the drug products.

NDA #	Status	Date	CT	Sponsor	Drug Name
N017559	AP	01-May-1981	1	Schering	Proventil (Albuterol) Mdl
N017853	AP	07-May-1982	3	Schering	Proventil Tablets
N018062	AP	19-Jan-1983	3	Schering	Proventil (Albuterol) Syrup
N018473	AP	01-May-1981	5	Glaxo Wellcome	Ventolin (Albuterol) MDI
N019112	AP	10-Jul-1986	5	Glaxo Wellcome	Ventolin Tab (Albuterol)
N019243	AP	14-Jan-1987	3	Schering	Proventil (Albuterol) Inhalation Solution
N019269	AP	16-Jan-1987	5	Glaxo Wellcome	Ventolin (Albuterol Sulfate) Sol Inhalation
N019383	AP	13-Jul-1987	3	Schering	Proventil (Albuterol Sulfate) Repetabs
N019489	AP	04-May-1988	3	Glaxo Wellcome	Ventolin Rotacaps Inhalation (Albuterol S04)
N019604	AP	23-Dec-1992	3	Muro Pharm	Volmax (Albuterol S04) Tablets Oros
N019621	AP	10-Jun-1987	5	Glaxo Wellcome	Ventolin Syrup (Albuterol Sulfate)
N019773	AP	23-Apr-1992	3	Glaxo Wellcome	Ventolin
N020291	AP	24-Oct-1996	4	Boehringer Ingelheim	Combivent (Albuterol Sulfate)
N020503	AP	15-Aug-1996	3	3m Pharmaceuticals	Proventil-HFA Inhalation Aerosol

CONSULTS:

Consult	Forward Date	Status	Comments
1. Establishment Evaluation (EER)	05-18-2000	Acceptable	Refer to page 105 of this review
2. Microbiology (HFD-160)	01-20-2000	Approval 05-10-2000	Refer to Microbiology Review #2, 05-10-2000 and page 92 of this review
3. Pharmacology (HFD-570)	05-12-2000	Not acceptable 05-25-2000	Refer to pages 7, 88 of this review.
4. Biometrics	-	-	Will be initiated if needed upon receipt of the updated stability data.
5. Methods Validation		Pending	See remarks in Section V/p 105 of this review.
6. Labeling & Nomenclature (OPDRA/HFD-400)	01-11-2000	Acceptable 04-27-2000	Refer to OPDRA review, 04-27-2000 See remarks in Section VI/p 105 of this review
7. Environmental Assessment	04-14-2000	Acceptable 05-18-2000	See remarks in Section VII/p 105 of this review

REMARKS/COMMENTS: See attached Review Notes

From GMP perspective, all the establishments that are involved in the manufacture of this drug product have been found acceptable by the Office of Compliance (see EERS report dated May 18, 2000).

CONCLUSIONS & RECOMMENDATIONS:

Several CMC deficiencies have been found in this NDA 20949 and supporting drug master files (DMFs) [redacted] and [redacted] for the components of container closure system. The holders of respective DMFs have been notified accordingly of the CMC comments pertaining to their product.

Consequently, NDA 20949 for AccuNeb™ (albuterol sulfate) Inhalation Solution, submitted by Dey Laboratories can not be approved until the CMC issues contained in the draft letter of this review and also in the CMC reviews of supporting DMFs [redacted] are completely addressed and resolved satisfactorily.

IS/
Vibhakar J. Shah, Ph.D. 06/02/2000
Review Chemist, DNDCCI (HFD-820)

cc:

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<input checked="" type="checkbox"/> HFD-570/Division File	<input checked="" type="checkbox"/> HFD-570/CSO/DHilfiker	<input checked="" type="checkbox"/> HFD-820/DD/JGibbs	

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Division of Pulmonary Drug Products

Chemist NDA Review

Review of Chemistry Manufacturing & Controls

FEB 26 1999

NDA No.: N 20949
CHEM. REVIEW: # 1

REVIEW COMPLETION DATE: January 31, 1999
REVIEWER: Vibhakar Shah, Ph.D.

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Original Submission (6 CMC Vol/57 Volumes)	March 27, 1998	March 30, 1998	April 08, 1998
Correspondence	May 04, 1998	May 08, 1998	May 12, 1998
Amendment (BZ)	May 18, 1998	May 19, 1998	May 28, 1998
Amendment (BZ)	June 09, 1998	June 10, 1998	June 16, 1998
Amendment (BZ)	June 19, 1998	June 24, 1998	June 29, 1998
Amendment (BC)	July 01, 1998	July 06, 1998	July 09, 1998
Amendment (BZ)	July 17, 1998	July 20, 1998	July 20, 1998

NAME & ADDRESS OF APPLICANT:

Dey Laboratories
2751 Napa Valley Corporate Drive
Napa, CA 94558
Tel: (707) 224-3200
Fax: (707) 224-3235

DRUG PRODUCT NAME:

Proprietary: Accuneb™ (proposed) Inhalation Solution.
Nonproprietary/USAN: Albuterol sulfate Inhalation Solution
Code Name/#: Not applicable
Chemical Type/Therapeutic Class: 5 S

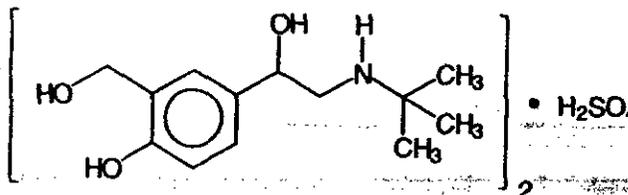
PHARMACOLOGICAL CATEGORY:

INDICATION: C
DOSAGE FORM: I
STRENGTHS: 0.042% (1.25 mg/3 mL), 0.021 % (0.62 mg/3 mL)
Maximum Daily Dose: 3 - 4x /day, i.e., TDI = 2.5 - 5 mg
ROUTE OF ADMINISTRATION: Oral-Inhalation through Nebulization
DISPENSED AS: Rx OTC
SPECIAL PRODUCTS: Yes No

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Chemical Name: 1,3-benzenedimethanol, α^1 -[[[(1,1-dimethylethyl)amino]-methyl]-4-hydroxy-, sulfate (2:1) salt, or α^1 -[tert-butylamino)methyl]-4-hydroxy-m-xylene- α,α' -diol sulfate (2:1) salt

Molecular Formula: $(C_{13}H_{21}NO_3)_2 \cdot H_2SO_4$
Molecular Weight: 576.71
CAS Registry No: [51022-70-9]



Albuterol sulfate (USP 23, p 39)

SUPPORTING DOCUMENTS:

A. DMFs:

DMF/Type	DMF Holder	Subject	LOA Date	Status	Reference
DMF Type II	/	Mfg. of Albuterol sulfate, USP	01-10-1997	Inadequate Def. Letter/ 02-26-1999	DMF Review #11, V.Shah/HFD-820, 02-25-1999 Refer to p. 96 of this Review
DMF Type III	/	/	05-12-1997	Inadequate Def Letter/ 01-25-1999	Chemist Review #2, V. Shah/HFD-820,12-23-1998
DMF Type III	/	/	06-18-1997	Inadequate Def Letter/ 01-25-1999	Chemist Review #1, V. Shah/HFD-820, 12-23-1998
DMF	/	/	05-21-1998	Inadequate Def Letter/ 01-25-1999	Chemist Review #1, V.Shah/HFD-820 01-08-1999

B. INDs/NDAs:

The following IND has been specified by the applicant in support of this application.

IND 44281 Albuterol sulfate Inhalation solution.

RELATED DOCUMENTS (if applicable): Numerous NDAs and ANDAs

There are numerous approved NDAs and ANDAs for for albuterol as an API in Inhalation Solutions, MDIs, DPIs, Aerosols, Tablets and syrups. The following list identifies the NDAs that have been approved in the Division of Pulmonary drug products (HFD-570) for albuterol as an API in the drug products.

<u>NDA #</u>	<u>Status</u>	<u>Date</u>	<u>CT</u>	<u>Sponsor</u>	<u>Drug Name</u>
N017559	AP	01-May-1981	1	Schering	Proventil (Albuterol) Mdi
N017853	AP	07-May-1982	3	Schering	Proventil Tablets
N018062	AP	19-Jan-1983	3	Schering	Proventil (Albuterol) Syrup
N018473	AP	01-May-1981	5	Glaxo Wellcome	Ventolin (Albuterol) Mdi
N019112	AP	10-Jul-1986	5	Glaxo Wellcome	Ventolin Tab (Albuterol)
N019243	AP	14-Jan-1987	3	Schering	Proventil (Albuterol) Inhalation Solution
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N020503	AP	15-Aug-1996	3	3m Pharmaceuticals	Proventil-HFA Inhalation Aerosol

CONSULTS:

CONSULT	Forward Date	Status	Comments
1. Establishment Evaluation (EER)	06-18-1998	Acceptable 10-19-1998	Refer to page # 35, 81 of this review
2. Microbiology	08-26-1998	Approvable 12-08-1998	Refer to page # 62 of this review
3. Pharmacology	12-16-1998	Not acceptable 01-11-1998	Refer to page # 12 of this review.
4. Biometrics	-	-	Will be initiated if needed upon receipt of the updated stability data.
5. Methods Validation		Pending	See remarks in Section V of this review.
6. Labeling & Nomenclature		Acceptable 10-06-1998	See remarks in Section VI of this review
7. Environmental Assessment		Acceptable	See remarks in Section VII of this review

REMARKS/COMMENTS: See attached Review Notes

The comment pertaining to the DMF [redacted] (albuterol sulfate USP) on page 06 of this review has been slightly modified to reflect the remarks/comment made on page 96 under the addendum section of this review. The draft comment 1a on p. 82 reflects this modified comment.

CONCLUSIONS & RECOMMENDATIONS:

Several CMC deficiencies have been found in this NDA 20949 and other supporting documents such as DMF [redacted] for the drug substance albuterol sulfate and DMFs [redacted] for the components of container closure system. The DMF holders of respective DMFs have been notified of the CMC comments pertaining to their product.

Consequently, NDA 20949 for Accuneb® (albuterol sulfate) Inhalation Solution, submitted by Dey Laboratories can not be approved until the CMC issues contained in the draft letter of this review and also in the CMC reviews of supporting DMFs [redacted] and [redacted] are completely addressed and resolved satisfactorily.

IS
Vibhakar J. Shah, Ph.D. 02-25-99
Review Chemist, DNDCII (HFD-820)

cc:

Org. NDA 20949
HFD-570/Division File
HFD-570/Chemist/VShah
HFD-570/CSO/DHilfiker
HFD-570/TL/GPoochikian

R/D Init by: GPoochikian / *3/26/99*
Document: n20949CMCRev1.doc
Filename: E:\CDER\Docs\DPDP570\NDAs\N20949\N20949CMCRev1.doc

NOT APPROVED

Vibhakar Shah, Ph. D.
Januaary 31, 1999

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Redacted 93

page(s) of trade secret.

and/or confidential

commercial information

(b4)

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: **NDA 20949/000** Priority: **5S** Org Code: **570**
Stamp: **30-MAR-1998** Regulatory Due: **30-APR-2001** Action Goal: District Goal: **01-MAR-2001**
Applicant: **DEY LABS** Brand Name: **ACCUNEB INHALATION SOLUTION**
2751 NAPA VALLEY CORPORATE DR Established Name:
NAPA, CA 94558 Generic Name: **ALBUTEROL SULFATE INHALATION SOLUTION**
Dosage Form: **LQI (LIQUID FOR INHALATION)**
Strength: **1.25MG/3ML; 0.62MG/3 ML**

FDA Contacts: **D. HILFIKER (HFD-570) 301-827-1050** , Project Manager
V. SHAH (HFD-570) 301-827-1050 , Review Chemist
G. POOCHIKIAN (HFD-570) 301-827-1050 , Team Leader

Overall Recommendation:

ACCEPTABLE on 01-FEB-2001 by S. FERGUSON (HFD-324) 301-827-0062
ACCEPTABLE on 18-MAY-2000 by J. D AMBROGIO (HFD-324) 301-827-0062
ACCEPTABLE on 19-OCT-1998 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment: **2938970** DMF No:
DEY LABORATORIES INC AADA No:
2751 NAPA VALLEY CORPORATE DR
NAPA, CA 94558

Profile: **SNI** OAI Status: **NONE** Responsibilities: **FINISHED DOSAGE MANUFACTURER**
Last Milestone: **OC RECOMMENDATION** **FINISHED DOSAGE RELEASE**
Milestone Date: **23-JAN-2001** **TESTER**
Decision: **ACCEPTABLE** **FINISHED DOSAGE STABILITY**
Reason: **BASED ON FILE REVIEW** **TESTER**
BASED ON PROFILE

Establishment:  DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE** Responsibilities: 
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **01-FEB-2001**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Establishment:  DMF No:
AADA No:

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Profile: CSN OAI Status: NONE Responsibilities:
Last Milestone: OC RECOMMENDATION
Milestone Date: 24-JAN-2001
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

APPEARS THIS WAY
ON ORIGINAL