

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

75-358

CHEMISTRY REVIEW(S)

Division of Pulmonary and Allergy Drug Products

Review of Pharmacology/Toxicology Data

Chemistry Consult: Chemistry consult dated February 9, 2000

Reviewer: VEWhitehurst

Review Date Completion: March 6, 2000

Information to be Conveyed to the Sponsor: No

HFD: HFD 570

NDA/ANDA: ANDA 75-358

Sponsor: Bausch and Lomb Pharmaceutical, Inc.
8500 Hidden River Parkway
Tampa, FL 33637

Drug: Albuterol Sulfate Inhalation Solution, 0.083%

Category: Beta-agonist

Indication: Treatment and relief of bronchospasm in patients with reversible obstructive airway disease and acute attacks of bronchospasms.

Route of Administration: Inhalation

Dose: Maximum daily dose is 10 mg or 0.2 mg/kg for a 50 kg person.

Related NDAs/DMFs: NDA 20-949; DMFs

Introduction and History:

This review is to respond to a chemistry consult (attached) requested by Harvey Greenberg, Project Manager, Division of Labeling and Program Support (HFD 615) to evaluate the safety of in the drug product. The contamination is from the overwrap/pouch system.

Toxicity:

Number of vials used per day: 4

ppm x 3 ml vials = approximately _____ x 4 vials /day = _____ or
_____ µg/kg for a 50 kg person.

OSHA/TWA/ACGIH daily permissible exposure limit (PEL): 20 ppm = 10 mg/kg.

Comment: Level of _____ Albuterol Sulfate Solution is qualified based on the _____ fold difference between exposure levels and the OSHA PEL.

Additional Factor:

Sponsor submits data which they state demonstrates that _____ is present in a currently marketed inhalation product (_____ er Solution) at concentrations equal to or greater than Bausch and Lomb's Albuterol Sulfate Inhalation Solution. The comparison of the concentrations of _____ in these 2 products is shown below:

Sample Description	Concentration
Maximum value observed for Albuterol Sulfate Inhalation Solution, 23 months old under accelerated (25±2°C) conditions	
Solution Lot # F6J025, 60 unit pouch expires 9/98 (approximately 22 months old assuming 24 months expiry)	
Solution Lot # F8F008, 60 unit pouch expires 6/00 (approximately 17 months old assuming 24 expiry)	
Solution Lot # F9G003, 60 unit pouch expires 7/01 (approximately 4 months assuming 24 months expiry)	

Comment: It is unclear from these data whether the concentration of _____ in _____ is an outlier or not, since it is quite different from the other 2 concentrations of _____. Additionally, it is unclear whether the method used for the analysis of _____ is valid.

Recommendation:

The level of _____ in Albuterol Sulfate Solution is qualified with _____ based on the _____ fold difference between exposure levels and the OSHA PEL.

Virgil Whitehurst
Virgil Whitehurst
Pharmacologist 3-9-00

CC:

1-00

Chemistry Closed

Office of Generic Drugs

Chemistry, Manufacturing and Controls Review

1. CHEMISTRY REVIEW NO. 6
2. ANDA# 75-358
3. NAME AND ADDRESS OF APPLICANT
Bausch and Lomb Pharmaceuticals (BLP)
Attention: Joseph B. Hawkins
8500 Hidden River Parkway
Tampa, FL 33637
4. LEGAL BASIS FOR SUBMISSION : 505j
5. SUPPLEMENT(s): N/A
6. PROPRIETARY NAME: N/A
7. NONPROPRIETARY NAME: Albuterol Sulfate Inhalation Solution, 0.083%
8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A
9. AMENDMENTS AND OTHER DATES:

Submission date	Submission type/Review Status
04/14/98	Original
04/28/98	New corresp.
11/06/98	Major Amendment
06/09/99	Minor Amendment
08/12/99	Fax Amendment
10/01/99	Sterility Information
11/04/99	Minor Amendment
11/24/99*	Minor Amendment
- 01/21/00*	Minor Amendment

*Subject to this review.

FDA Responses date	Response type
05/13/98	Accept for filing
05/13/98	EERs issued
05/27/98	Labeling review-Deficiencies
07/23/98	Bioequivalency -Acceptable
12/02/98	Labeling(2 nd review)-Deficiencies
05/24/99	EER is acceptable
06/22/99	Labeling(3 rd review)-Deficiencies
07/07/99	CMC NA (fax)
07/29/99	MV report issued-acceptable
08/18/98	Labeling -Accepted
09/15/99	CMC Minor
10/20/99	Micro-Acceptable
12/10/99	CMC Minor (
12/16/99	Telecon

10. PHARMACOLOGICAL CATEGORY

beta2-adrenergic bronchodilator

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

NDA #/Product Name		Innovator	
N019773/ Ventolin Nebules® Inhalation Solution		Allen & Hansburys Division of Glaxo, Inc.	
DMF number	DMF type	DMF holder	LOA(s)

13. DOSAGE FORM: Solution

14. POTENCY

Strength	Strength (units)
0.83	mg/mL

15. CHEMICAL NAME AND STRUCTURE

See USP or CR#1.

16. RECORDS AND REPORTS

N/A

17. COMMENTS:

Page (s)

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Contain Trade Secret,

Commercial/Confidential

Information and are not

releasable.

Chem Rev

1/31/00

Addendum to Chemistry Review #6

ANDA Number: 75-358

Drug: Albuterol Sulfate Inhalation Solution

Firm: Bausch and Lomb Pharmaceutical, Inc..

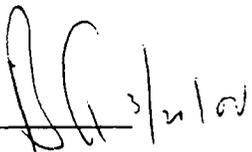
Background:

This ANDA was CMC closed on 01/31/00 and was pending for a consultation regarding the safety issue of

The results from the consultation are OK (see attached Pulmonary Consult dated 03/09/00).

During this period, a major DMF revision was submitted from the DMF holder (03/01/00). The DMF has been reviewed. An IR letter is sent to the DMF holder to request some additional information regarding the impurity controls. Those requirements are in addition to the current USP spec. in this case, it won't effect the approval of this ANDA.

The ANDA is approvable.



Bing Cai
Review Chemist



Mike Smela
Team Leader