

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

205636Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

MEMORANDUM



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

DATE: March 5, 2015
TO: NDA 205636
FROM: Vinayak B. Pawar, Ph.D., Sr. Review Microbiologist, CDER/OPQ/DMA
THROUGH: CDR Paul Dexter, M.S., Acting Chief, Branch I, CDER/OPQ/DMA
cc: Leila Hann, Sr. Regulatory Project Manager, CDER/OND/ODEII/DPA
SUBJECT: Product Quality Microbiology assessment of Microbial Limits for Albuterol Sulfate Inhalation Powder (Albuterol Multi-Dose Dry Powder Inhaler). [Submission Date: January 20, 2015]

Drug product: Albuterol Sulfate Inhalation Powder (Albuterol Multi-Dose Dry Powder Inhaler).

Submission Date: January 20, 2015

Submission Provides for: Sponsor's response to FDA information request dated May 5, 2014. Questions pertained to Section 1.11.1 Quality Information Amendment and subsequent revision of the drug product specifications.

FDA Information Request:

1. Revise the drug product specification as follows:

FDA Comment:

a. Tighten the acceptance criterion for Net Content (Fill) Weight to (b) (4)

b. Tighten the acceptance criterion for Assay (Total Drug Content per inhaler) to (b) (4) mg of albuterol base/inhaler.

c. Revise the acceptance criteria for the APSD as highlighted below.

For n=5 inhalers, perform determinations on each inhaler at beginning and end.

Report mass deposition for each individual determination in 4 groups:

Group 1 (MP/IP, Pre-Separator) (b) (4) µg

Group 2 (Stage 1, 2) (b) (4) µg

Group 3 (Stage 3, 4, & 5) (b) (4) µg

Group 4 (Stage 6, 7 & MOC) (b) (4) µg

CMC Response: Teva's response to the above was acceptable.

Microbiology Product quality Comment:

According to the original Microbiology Product Quality review dated May 29, 2014, "The Microbial Limits specification for Albuterol Sulfate Inhalation Powder (Albuterol Multi-Dose Dry Powder

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Inhaler) was acceptable from Product Quality Microbiology perspective. Therefore, this non-sterile drug product submission was recommended for approval from the standpoint of product quality microbiology". An amendment was received on January 20, 2015 containing revised drug product specifications. Upon review of this amendment it is concluded that the CMC revisions to the specifications do not affect the microbiology product quality. Therefore, no further review is required.

END

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/s/

VINAYAK B PAWAR
03/31/2015

PAUL L DEXTER
03/31/2015

MEMORANDUM



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DATE: 29 May 2014

TO: NDA 205636

FROM: Bryan S. Riley, Ph.D.
Team Leader (Acting)
OPS/New Drug Microbiology Staff

THROUGH: John W. Metcalfe, Ph.D.
Senior Review Microbiologist
OPS/New Drug Microbiology Staff

cc: Leila P. Hann
Regulatory Project Manager
OND/DPARP

SUBJECT: Product Quality Microbiology assessment of Microbial Limits for
Albuterol Sulfate Inhalation Powder [Submission Date: 5 May 2014]

The Microbial Limits specification for Albuterol Sulfate Inhalation Powder is acceptable from a Product Quality Microbiology perspective. Therefore, this submission is recommended for approval from the standpoint of product quality microbiology.

Albuterol Sulfate Inhalation Powder is for oral inhalation.

The drug product is tested for Microbial Limits at release using a method consistent with USP Chapter <61> (Microbiological Examination of Non-sterile Products: Microbial Enumeration Tests) and <62> (Microbiological Examination of Non-sterile Products: Tests for Specified Microorganisms). The Microbial Limits acceptance criteria are consistent with USP Chapter <1111> (Microbiological Examination of Non-sterile Products: Acceptance Criteria for Pharmaceutical Preparations and Substances for Pharmaceutical Use).

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Table 1 – Microbial Limits Specifications

Test	Acceptance Criteria
Total Aerobic Microbial Count (USP <61>)	NMT ^{(b) (4)} CFU/g
Total Yeast and Mold Count (USP <61>)	NMT ^{(b) (4)} CFU/g
<i>Pseudomonas aeruginosa</i> (USP <62>)	Absent in 1 g
<i>E. coli</i> (USP <62>)	Absent in 1 g
<i>Staphylococcus aureus</i> (USP <62>)	Absent in 1 g
Bile-tolerant Gram Negative Bacteria (USP <62>)	Absent in 1 g

The Microbial Limits test methods were verified to be appropriate for use with the drug product following procedures consistent with those in USP Chapter <61> and <62>.

The drug product will also be tested for Microbial Limits at 0, 6, 12, 18, 24 and 36 months as part of the post-approval stability protocol.

ADEQUATE

Reviewer Comments – The microbiological quality of the drug product is controlled via a suitable testing protocol.

END

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/s/

BRYAN S RILEY
05/29/2014

JOHN W METCALFE
05/29/2014
I concur.