

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

205108Orig1s000

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: 31 January 2014

TO: NDA 205108

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

THROUGH: Stephen E. Langille, Ph.D.
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cc: Russell Fortney, R.Ph.
Regulatory Health Project Manager
OND/Division of Cardiovascular and Renal Products

SUBJECT: Product Quality Microbiology assessment of Microbial Limits for Sotalol Hydrochloride Oral Solution [Submission Date: 23 December 2013]

The Microbial Limits specification for Sotalol Hydrochloride Oral Solution is acceptable from a Product Quality Microbiology perspective. Therefore, this submission is recommended for approval from the standpoint of product quality microbiology.

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).

MEMORANDUM

Table 1 – Microbial Limits Specifications

Test	Acceptance Criteria
Total Aerobic Microbial Count (USP <61>)	NMT (b) (4)
Total Yeast and Mold Count (USP <61>)	NMT
<i>E. coli</i> (USP <62>)	Absent in 1 mL
<i>Salmonella</i> species (USP <62>)	Absent in 10 mL
<i>Staphylococcus aureus</i> (USP <62>)	Absent in 1 mL
<i>Pseudomonas aeruginosa</i> (USP <62>)	Absent in 1 mL
<i>Burkholderia cepacia</i> *	Absent in 1 mL

* = A method for detecting the presence of *B. cepacia* is not included in the current USP Chapter <62>. However, the proposed *B. cepacia* method was described and verified for use with the drug product by demonstrating the ability to recover *B. cepacia* in the presence of the product. The purified water used to manufacture the drug product is also tested for *B. cepacia* (absent in 100 mL).

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 was also tested for antimicrobial effectiveness using the test method in USP Chapter <51> on product formulated at the minimum acceptable level of Sodium Benzoate (b) (4). The product with (b) (4)% Sodium Benzoate met the acceptance criteria for a category 3 drug product (Oral products other than antacids, made with aqueous bases or vehicles). Six registration batches of the drug product (three 250mL fills and three 480 mL fills) were also tested and met the acceptance criteria in USP <51>.

The drug product will also be tested for Microbial Limits and Antimicrobial Effectiveness annually 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 and the multi-dose drug product is adequately preserved.

END

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/s/

BRYAN S RILEY
02/04/2014

STEPHEN E LANGILLE
02/04/2014