

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**207925Orig1s000**

**MICROBIOLOGY / VIROLOGY REVIEW(S)**

# MEMORANDUM



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

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**DATE:** 10 February 2015

**TO:** NDA 207925

**FROM:** Bryan S. Riley, Ph.D.  
Branch Chief (Acting)  
OPQ/OPF/Div. of Microbiology Assessment

**THROUGH:** John W. Metcalfe, Ph.D.  
Branch Chief (Acting)  
OPQ/OPF/Div. of Microbiology Assessment

**cc:** Angela H. Ramsey, RN, MSN, MPH  
Senior Program Management Officer  
OND/DPARP

**SUBJECT:** Product Quality Microbiology assessment of Microbial Limits for KALYDECO (ivacaftor granules) [Submission Date: 17 September 2014]

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**The microbial controls for KALYDECO (ivacaftor granules) are acceptable from a Product Quality Microbiology perspective. Therefore, this submission is recommended for approval from the standpoint of product quality microbiology.**

Ivacaftor granules are (b) (4) mixed with soft food and then administered orally.

The drug product will not be tested for Microbial Limits at release but will be tested on stability (0, 12, 24 and 36 months) 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 (b) (4)

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 manufacturing process for the drug product (b) (4) components (Ivacaftor (b) (4), Lactose monohydrate USP/NF, Mannitol USP/NF, Croscarmellose sodium USP/NF and Magnesium stearate USP/NF) are controlled for microbial content. Six batches of the drug product (b) (4) were tested for microbial limits at release and on stability and met the acceptance criteria.

ADEQUATE

**Reviewer Comments – The (b) (4) nature of the manufacturing process and the microbial control of the drug product components combine to minimize the risk to the drug product from a microbial standpoint. The acceptable microbial limits test results achieved to date also demonstrate that the microbial control is acceptable and routine release testing is unnecessary.**

END

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/s/  
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BRYAN S RILEY  
02/11/2015

JOHN W METCALFE  
02/11/2015  
I concur.