CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

206947Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

M E M O R A N D U M

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

DATE: 06 November 2014

TO: NDA 206-947

FROM: Jessica G. Cole, PhD
Review Microbiologist
CDER/OPS/New Drug Microbiology Staff
(301) 796-5148

THROUGH: Bryan Riley, PhD
Microbiology Team Leader
CDER/OPS/New Drug Microbiology Staff

cc: Deanne Varney
Project Manager
CDER/OND/OHOP/DOPII

SUBJECT: Product Quality Microbiology assessment of Microbial Limits for Lenvatinib [Submission Date: 14 August 2013]

The Microbial Limits specification for Lenvatinib 10 mg and 4 mg capsule is acceptable from a Product Quality Microbiology perspective. Therefore, this submission is recommended for approval from the standpoint of product quality microbiology.

Lenvatinib is a capsule for oral administration.

Information request dated 10 October 2014

1. You propose to perform [redacted] (b) (4) However, microbial limits testing may be omitted from the product release specification provided adequate upstream microbiological controls are established and documented. If you wish to omit the microbial limits specification, more information on your process is needed. Address the following points.
    1. Identify and justify critical control points in the manufacturing process that could affect microbial load of the drug product. This should include the maximum processing time for the [redacted] (b) (4) step.
    2. If applicable, describe microbiological monitoring and acceptance criteria for the critical

control points that you have identified. Verify the suitability of your testing methods for your drug product. Conformance to the acceptance criteria established for each critical control point should be documented in the batch record in accordance with 21 CFR 211.188.

3. Describe activities taken when microbiological acceptance criteria are not met at control points.

If you choose to omit microbial limits testing for release, then remove the microbial limits tests and acceptance criteria from the drug product release specification. Alternatively, you may retain a microbial limits specification for product release, but testing must be performed on every lot of drug product produced.

Please submit a revised drug product release specification for whichever microbial limits testing alternative that you select.

Summary of response received 06 November 2014

The applicant now proposes microbiological release testing.

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). The specification includes NMT (b) (4) CFU/g total aerobic microbial count, NMT (b) (4) CFU/g total yeast and mold count, and the absence of *Escherichia coli, Pseudomonas aeruginosa,* and *Staphylococcus aureus.*

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 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.

END

MEMORANDUM

Jessica Cole -S

Digitally signed by Jessica Cole -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Jessica Cole -S, 0.9.2342.19200300.100.1.1=2000397920
Date: 2014.11.07 07:41:09 -05'00'

Bryan S. Riley -S

Digitally signed by Bryan S. Riley -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Bryan S. Riley -S, 0.9.2342.19200300.100.1.1=1300138775
Date: 2014.11.07 08:09:12 -05'00'

PRODUCT QUALITY MICROBIOLOGY NON-STERILE

DRUG PRODUCT FILING CHECKLIST

NDA Number: 206-947 **Applicant:** Eisai, Inc. **Letter Date:** 14 August 2014

Drug Name: Lenvatinib **NDA Type:** 505(b)(1) NME **Stamp Date:** 14 August 2014

Dosage Form: Capsule **Reviewer:** Jessica G. Cole, PhD

The following are necessary to initiate a review of the NDA application:

	Content Parameter	Yes	No	Comments
1	Is the product quality microbiology information described in the NDA and organized in a manner to allow substantive review to begin? Is it legible, indexed, and/or paginated adequately?	X		
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		(b) (4)
3	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		(b) (4) is proposed with microbial enumeration on stability
4	Has the applicant submitted the results of analytical method verification studies?	X		
5	Has the applicant submitted preservative effectiveness studies (if applicable)?			Not applicable
6	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: This product is indicated for treatment of thyroid cancer and was granted Orphan Designation. There is a 10 mg and a 4 mg capsule associated with this NDA.

Product Quality Microbiology Information Request:

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Jessica G. Cole, PhD	18 September 2014
Reviewing Microbiologist	Date
Bryan Riley, PhD	
Microbiology Team Leader	Date

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JESSICA COLE
09/25/2014

BRYAN S RILEY
09/25/2014
I concur.