CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204768Orig1s000

MICROBIOLOGY/VIROLOGY REVIEW(S)

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

DATE: 13 May 2013

TO: NDA 204768

FROM: Erika Pfeiler, Ph.D.
Microbiologist

THROUGH: John Metcalfe, Ph.D.
Senior Review Microbiologist

cc: Kimberly Compton

SUBJECT: Product Quality Microbiology assessment of Microbial Limits for (b) (4) [Submission Date: 30 April 2013]

The NDA (b) (4) does not include a Microbial Limits release specification; however, the applicant provides a suitable rationale for the exclusion of this testing. Therefore, this submission is recommended for approval from the standpoint of product quality microbiology.

(b) (4) is a capsule for oral administration.

The applicant presents a rationale for waiving Microbial Limits testing on product release, stating that that the finished drug product is inhibitory towards microbial growth. The application provides data from six primary stability batches demonstrating that no microbial growth is detected in the finished product over a 12 month period. In addition to its inhibitory properties towards microbial growth, this product is produced (b) (4) and excipients (b) (4) are monitored by vendors for microbial limits and the absence of objectionable microorganisms. This product presents a low risk for microbial proliferation during processing and in its finished form.

The drug product will be tested for Microbial Limits annually as part of the post-approval stability protocol 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 for stability testing are consistent with USP Chapter <1111> (Microbiological Examination of Non-

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sterile Products: Acceptance Criteria for Pharmaceutical Preparations and Substances for Pharmaceutical Use). These limits include NMT (b) (4) total aerobic microbial count, NMT (b) (4) total combined yeasts/molds count, and the absence of *Escherichia coli* (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 Chapters <61> and <62>.

ADEQUATE

Reviewer Comments – The applicant's proposal to waive microbial limits testing for product release is acceptable. Microbial Limits testing will be performed as a part of the stability program.

END

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/s/

ERIKA A PFEILER
05/13/2013

JOHN W METCALFE
05/13/2013
I concur.