CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

205353Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)
DATE: 29 May 2014

TO: NDA 205353

FROM: Erika Pfeiler, Ph.D.
Microbiologist
CDER/OPS/NDMS

THROUGH: John Metcalfe, Ph.D.
Senior Review Microbiologist
CDER/OPS/NDMS

cc: Diane Hanner
Senior Program Manager
CDER/OND/OHOP/DHP

SUBJECT: Product Quality Microbiology assessment of Microbial Limits for FARYDAK® (proposed) [Submission Date: 22 March 2014]

The microbial limits specification for FARYDAK® (proposed) is acceptable from a Product Quality Microbiology perspective and is recommended for approval from the standpoint of product quality microbiology.

FARYDAK® (proposed) is a capsule for oral administration with 10 mg, 15 mg, and 20 mg presentations.

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). Recommended acceptance criteria in USP <1111> for product of this type include a total aerobic microbial count of $10^3$ CFU/g, a total yeast and mold count of $10^2$ CFU/g, and the absence of *Escherichia coli* per gram.

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>.

Reference ID: 3514577
MEMORANDUM

The drug product will also be tested for microbial limits annually as part of the post-approval stability protocol at initial, 12, and 36 month time points.

ADEQUATE

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

END

12 May 2014 Information Request

If a drug product release specification includes tests and acceptance criteria for a given attribute, 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. At a minimum, you should define

2. 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.

In addition to these points, you should minimally perform microbial limits testing at the initial stability testing time point. Provide an updated stability schedule to reflect this testing.

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.

21 May 2014 Response

The applicant agreed to perform microbial limits release tests for all drug product batches. This response was adequate to complete the review.
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ERIKA A PFEILER
05/29/2014

JOHN W METCALFE
05/29/2014

I concur.