CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

206544Orig1s000

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: 16 July 2015

TO: NDA 206544

FROM: Erika Pfeiler, Ph.D.
CDER/OPQ/OPF/DMA

THROUGH: Stephen Langille, Ph.D.
CDER/OPQ/OPF/DMA

cc: Luz Rivera
CDER/OPQ/OPRO/DRBPMII/RBPMBIV

SUBJECT: Product Quality Microbiology assessment of Microbial Limits for Morphine Sulfate abuse-resistant, extended-release tablets [Submission Date: 21 November 2014]

The applicant proposes a waiver of microbial limits testing for product release, and provides a suitable rationale to support the waiver. Therefore, this submission is recommended for approval from the standpoint of product quality microbiology.

The subject drug product is a coated tablet for oral administration, with 15 mg, 30 mg, 60 mg, and 100 mg presentations proposed.

The applicant proposes a waiver of microbial limits testing for product release. The rationale for this proposal states that the applicant has identified critical control points for the manufacturing process, including (b) (4) is used in manufacturing) and excipient quality (microbial limits of excipients are monitored). The manufacturing facility employs an environmental monitoring program.

Microbial limits testing was performed on registration batches of drug product 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). These criteria state the product's TAMC should be NMT 10^3 CFU/g, the TYMC should be NMT 10^2 CFU/g, and

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Escherichia coli should be absent in 1 g. 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>.

(b) (4)

The drug product is tested for microbial limits (b) (4) as a part of the post-approval stability program.

ADEQUATE

Reviewer Comments – (b) (4) content, is the preferred method to assess the likelihood of microbial proliferation in a substance. However, release testing of (b) (4) (b) (4) is taken with the other microbial control strategies proposed by this applicant, the proposed plan is adequate to control the introduction and proliferation of microorganisms into the drug product.

END

Filing Communication Information Request

1. *Your application proposes a waiver of microbial limits testing for product release and stability. You include a release acceptance criterion for (b) (4) (b) (4) of (b) (4)%. What is the corresponding (b) (4) (b) (4) ? You are encouraged to change your release specification (b) (4) (b) (4) more closely indicates the potential for microbial growth than (b) (4) content does.*

2. *You state that microbial limits testing was performed on registration batches of the drug product using methods described in USP <61> and USP <62>. State whether these methods were verified for use with the drug product.*

3. *You should minimally perform microbial limits testing at the initial stability testing time point. Provide an updated stability schedule to reflect this testing.*

29 April 2015 and 15 May 2015 Response
The applicant provided the requested information, including a commitment to investigate the use of (b) (4) as a product release criterion.

MEMORANDUM

Erika A. Pfeiler -S

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Date: 2015.07.16 07:43:14 -04'00'

Stephen E. Langille -A

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Date: 2015.07.16 07:46:00 -04'00'