

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**205583Orig1s000**

**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:** 01 August 2013

**TO:** NDA 205583

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

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

**cc:** ShinYe Chang  
CDER/OND/ODEI/DPP

**SUBJECT:** Product Quality Microbiology assessment of Microbial Limits for Desvenlafaxine Fumarate Tablet, Extended Release (50 mg and 100 mg) [Submission Date: 28 March 2013]

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**The Microbial Limits specification for the Desvenlafaxine Fumarate Tablet, Extended Release is acceptable from a Product Quality Microbiology perspective. Therefore, this submission is recommended for approval from the standpoint of product quality microbiology.**

Desvenlafaxine Fumarate Tablet, Extended Release is for oral administration.

The applicant proposes a waiver of microbial limits for drug product release testing, and provides a rationale for this waiver. The drug product is produced using (b) (4). The tablet coating is also prepared using (b) (4). The presence of (b) (4) in the manufacturing process limits the opportunity for microbial growth. There are in-process and release specifications of (b) (4) for the drug product. Some excipients are monitored for microbial limits and the absence of specific microorganisms based on monograph specifications (microcrystalline cellulose NF, magnesium stearate NF, (b) (4).) Environmental monitoring is performed in production areas on a monthly or biweekly basis, with alert limits of NMT (b) (4)/plate and action limits of NMT (b) (4)/plate.

The drug product will be tested for microbial limits annually as part of the post-approval stability protocol. The protocol states that microbial limits testing will be performed at 0 and 6 months for product held under accelerated conditions (40°C/75% RH) and at 0, 12, 24, and 36 months for

## MEMORANDUM

product held under long-term (25°C/60% RH.) Testing will be performed using methods 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-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* in (b) (4). Microbial limits testing stability data were presented both drug product strengths, all acceptance criteria were met.

One information request was sent to the applicant as part of the filing communication:

*29 May 2013 Information Request*

*You propose waiving microbial limits release testing for your drug product. This proposal may be acceptable provided adequate (b) (4) are established and documented. 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.*
- 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.*

*31 July 2013 Response*

*The applicant submitted information that was adequate to complete the review.*

### 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/  
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ERIKA A PFEILER  
08/01/2013

JOHN W METCALFE  
08/01/2013  
I concur.

## PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

**NDA Number:** 205583      **Applicant:** Sun Pharma Global FZE      **Letter Date:** 28 March 2013

**Drug Name:** Desvenlafaxine Fumarate Tablet, Extended Release      **NDA Type:** 505(b)(2)      **Stamp Date:** 28 March 2013

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		
3	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?		X	See comments.
4	Has the applicant submitted the results of analytical method verification studies?		X	See comments.
5	Has the applicant submitted preservative effectiveness studies (if applicable)?			N/A
6	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: The proposed drug product is a solid oral film-coated tablet that is produced using [REDACTED] <sup>(b) (4)</sup>. The applicant did not provide microbial limits acceptance criteria for product release, but provided acceptance criteria and testing methods for microbial limits in the stability program. More information on the process is needed to determine if a waiver of release microbial limits testing is acceptable for this product.

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Erika Pfeiler, Ph.D.  
Microbiologist

Date

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John Metcalfe, Ph.D.  
Senior Microbiology Reviewer

Date

Please provide the following comments to the applicant:

You propose waiving microbial limits release testing for your drug product. This proposal may be acceptable provided adequate (b) (4) are established and documented. 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.
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.

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/s/  
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ERIKA A PFEILER  
05/09/2013

JOHN W METCALFE  
05/10/2013  
I concur.