CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

205831Orig1s000

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: 20 January 2015

TO: NDA 205831

FROM: John W. Metcalfe, Ph.D.
Senior Review Microbiologist
CDER/OPS/New Drug Microbiology Staff

THROUGH: Bryan S. Riley, Ph.D.
Team Leader (Acting)
CDER/OPS/New Drug Microbiology Staff

cc: ShingYe Chang
Senior Regulatory Project Manager
CDER/OND/ODEI/DPP

SUBJECT: Product Quality Microbiology assessment of Microbial Limits for methylphenidate hydrochloride extended release capsules [Submission Date: 18 June 2014; Amendment Date: 12 January 2015]

The Microbial Limits specification for methylphenidate hydrochloride extended release capsules is acceptable from a Product Quality Microbiology perspective. Therefore, this submission is recommended for approval from the standpoint of product quality microbiology.

Methylphenidate hydrochloride extended release capsules is a Capsule for oral administration.

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 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.

The acceptance criteria for this testing are as follows:

Total Aerobic Microbial Count: NMT (b) (4)
Total Combined Molds and Yeasts: (b) (4)
Salmonella species: Absence
Escherichia coli: Absence
Pseudomonas aeruginosa: Absence
Staphylococcus aureus: Absence

ADEQUATE

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

END

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/s/

JOHN W METCALFE
01/20/2015

BRYAN S RILEY
01/20/2015
I concur.

PRODUCT QUALITY MICROBIOLOGY NON-STERILE

DRUG PRODUCT FILING CHECKLIST

NDA Number: 205831 **Applicant:** Rhodes Pharmaceuticals, L.P. **Letter Date:** 18 June 2014

Drug Name: Methylphenidate Hydrochloride Extended Release Capsules **NDA Type:** 505(b)(2) **Stamp Date:** 18 June 2014

Dosage Form: Capsule **Reviewer:** John W. Metcalfe, 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	The NDA does not include any product quality microbiology information
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		There is a description of the manufacturing process, but there is no information regarding microbiological control
3	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?		X	
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 to drug product
6	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: There is a Microbiology Information Request on page 2 of this review.

18 August 2014

John W. Metcalfe, Ph.D. Date
Senior Microbiology Reviewer, CDER/OPS/NDMS

18 August 2014

Bryan S. Riley, Ph.D. Date
Team Leader (Acting), CDER/OPS/NDMS

Microbiology Information Request to be Forwarded to the Applicant

[redacted] (b) (4) 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.

    a. Define the maximum processing time for the [redacted] (b) (4)

    b. Define the maximum holding time for the [redacted] (b) (4) (s)

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, address the following:

1. Provide the results of microbial limits testing performed on exhibit or stability batches of the drug product.

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

3. In the absence of historical data, you should perform quarterly microbial limits testing on stability batches for the first year of stability. Following the first year, testing may be performed annually.

In lieu of the above information, provide updated drug product release and stability specifications that include testing for microbial enumeration (USP<61>) and specified organisms (USP<62>) with acceptance criteria consistent with USP<1111>. Include data summaries demonstrating method suitability of the microbiological test methods with the drug product.

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/s/

JOHN W METCALFE
08/18/2014

BRYAN S RILEY
08/18/2014
I concur.