

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**203629Orig1s000**

**MICROBIOLOGY / VIROLOGY REVIEW(S)**

# Product Quality Microbiology Review

September 6, 2012

**NDA:** 203629/N000

**Drug Product Name**

**Proprietary:** Not Determined

**Non-proprietary:** Neostigmine Methylsulfate Injection, USP

**Review Number:** 1

**Dates of Submission(s) Covered by this Review**

Submit	Received	Review Request	Assigned to Reviewer
December 28, 2012	December 29, 2012	January 12, 2011	January 19, 2011

**Submission History (for amendments only) – N/A**

**Applicant/Sponsor**

**Name:** APP Pharmaceuticals – Fresenius Kabi Group

**Address:** 1501 E Woodfield Road, Schaumburg, IL 60173

**Representative:** James Harn, Manager of RA

**Telephone:** 847-517-5767

**Name of Reviewer:** Vinayak B. Pawar, Ph.D.

**Conclusion:** Recommend approval.

## Product Quality Microbiology Data Sheet

- A.**
- 1. TYPE OF SUBMISSION:** Original NDA
  - 2. SUBMISSION PROVIDES FOR:** Neostigmine Methylsulfate
  - 3. MANUFACTURING SITE:** APP Pharmaceuticals, Grand Island, NY 14072.
  - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** [REDACTED]<sup>(b) (4)</sup> injectable, 0.5 mg/mL and 1.0 mg/mL, both in a 10 mL multiple dose vial.
  - 5. METHOD(S) OF STERILIZATION:** [REDACTED]<sup>(b) (4)</sup>
  - 6. PHARMACOLOGICAL CATEGORY:** A reversal agent to the neuromuscular blocking effects of non-depolarizing muscle relaxants.
- B. SUPPORTING/RELATED DOCUMENTS:** None
- C. REMARKS:** The New Drug Application is submitted in accordance with 505(b)(2) to seek marketing approval of Neostigmine Methylsulfate injection, USP. The application is an eCTD submission.

**filename:** N203629R1

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**Executive Summary**

**I. Recommendations**

- A. **Recommendation on Approvability** – Recommend approval.
- B. **Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** – N/A

**II. Summary of Microbiology Assessments**

- A. **Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** –  <sup>(b) (4)</sup>  

- B. **Brief Description of Microbiology Deficiencies** - None
- C. **Assessment of Risk Due to Microbiology Deficiencies** – N/A

**III. Administrative**

- A. **Reviewer's Signature** \_\_\_\_\_  
**Vinayak B. Pawar, Ph.D.**
- B. **Endorsement Block** \_\_\_\_\_  
**John W. Metcalfe, Ph.D.**
- C. **CC Block**  
N/A

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/s/  
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VINAYAK B PAWAR  
09/10/2012

JOHN W METCALFE  
09/10/2012  
I concur.

## PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

**NDA Number:** 203629      **Applicant:** APP Pharmaceuticals **Letter Date:** 12/28/2011

**Drug Name:** Neostigmine      **NDA Type:** Original NDA      **Stamp Date:** 12/29/2011  
Methylsulfate USP Injection

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		Manufacturing Process and Controls, Section 3.2.P.3.3.
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		Process Validation & Evaluation, Section 3.2.P.3.5.
4	Are any study reports or published articles in a foreign language? If yes, has the translated version been included in the submission for review?		X	
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?	X		APE: N/A. CCI: Section 3.2.P.2.
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		Drug product Specifications & Methods Validation in Micro-Validation Pkg.
7	Has the applicant submitted the results of analytical method verification studies?	X		COA: Lots R341-001, 003, 007 &009.
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?		X	N/A
9	Is this NDA fileable? If not, then describe why.	X		

**Additional Comments:** The drug product is (b) (4) and conforms to the formulation and controls specified by USP monograph. Although there are no filing issues, per ONDQA, the manufacturing facility has been flagged for cGMP violations; OC is preparing Warning Letter as of 10/17/11 & 01/03/12 per CMS information.

*Vinayak B. Pawar, Ph.D., Sr. Review Microbiologist*

**Date**

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*John W. Metcalfe, Ph.D., Sr. Review Microbiologist*

**Date**

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/s/  
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VINAYAK B PAWAR  
02/22/2012

JOHN W METCALFE  
02/22/2012  
I concur.