

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**204640Orig1s000**

**MICROBIOLOGY / VIROLOGY REVIEW(S)**

# Product Quality Microbiology Review

25 November 2013

**NDA: 204640**

## Drug Product Name

**Proprietary:** Adrenalin<sup>®</sup> Injection

**Non-proprietary:** Epinephrine Injection, USP

**Review Number: 1**

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

Submit	Received	Review Request	Assigned to Reviewer
07 MAR 2012	07 MAR 2012	N/A	N/A*
02 AUG 2013	02 AUG 2013	07 AUG 2013	7 AUG 2013
14 AUG 2013	14 AUG 2013	N/A	N/A
01 NOV 2013	01 NOV 2013	N/A	N/A

\*See Remarks, Page 2

## Applicant/Sponsor

**Name:** JHP Pharmaceuticals, LLC

**Address:** Morris Corporate Centre 2  
One Upper Pond Road  
Building D, 3<sup>rd</sup> Floor  
Parsippany, NJ 07054

**Representative:** Steve Richardson, VP Scientific and Regulatory Affairs

**Telephone:** 973-658-3561

**Name of Reviewer:** Erika Pfeiler, Ph.D.

**Conclusion:** Recommended for Approval

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## Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** 505(b)(2)
  2. **SUBMISSION PROVIDES FOR:** Marketing of a sterile drug
  3. **MANUFACTURING SITE:** JHP Pharmaceuticals LLC  
870 Parkdale Road  
Rochester, MI 48307
  4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
    - Sterile aqueous solution, 30 ml (multiple use) amber glass vials
    - Intramuscular or subcutaneous injection
    - 1 mg/ml
  5. **METHOD(S) OF STERILIZATION:** [REDACTED] (b) (4)  
[REDACTED]
  6. **PHARMACOLOGICAL CATEGORY:** Treatment for severe anaphylactic reaction
- B. **SUPPORTING/RELATED DOCUMENTS:** Microbiology Review 24 of DMF [REDACTED] (b) (4) (26 April 2013)

C. **REMARKS:**

This application is a resubmission. The subject drug product was originally part of NDA 204200, which was split, and NDA 204640 was created with a retroactive date of 07 March 2012. NDA 204640 was refused for filing by FDA on 20 September 2012 due to nonpayment of user fees. The NDA was resubmitted on 02 August 2013 and the relevant quality microbiology information (same as what was submitted for NDA 204200) was submitted on 14 August 2013. This application was submitted in the eCTD format.

**filename:** N204640R1.doc

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## **Executive Summary**

### **I. Recommendations**

**A. Recommendation on Approvability** - Recommended for 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** - Product is sterilized by (b) (4)

**B. Brief Description of Microbiology Deficiencies** – N/A

**C. Assessment of Risk Due to Microbiology Deficiencies** – N/A

**D. Contains Potential Precedent Decision(s)**-  Yes  No

### **III. Administrative**

**A. Reviewer's Signature** \_\_\_\_\_  
Erika Pfeiler, Ph.D.  
Microbiologist

**B. Endorsement Block** \_\_\_\_\_  
John Metcalfe, Ph.D.  
Senior Microbiology Reviewer

**C. CC Block**  
N/A

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/s/  
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ERIKA A PFEILER  
11/25/2013

JOHN W METCALFE  
11/25/2013  
I concur.

## PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

**NDA Number:** 204640

**Applicant:** JHP  
Pharmaceuticals, LLC

**Letter Date:** 02 August 2013

**Drug Name:** Adrenalin  
Injection, 1 mg/ml

**NDA Type:** 505(b)(2)

**Stamp Date:** 02 August 2013

The following are necessary to initiate a review of the NDA application:

	<b>Content Parameter</b>	<b>Yes</b>	<b>No</b>	<b>Comments</b>
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 protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		See comments
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?			N/A, the submission is in English.
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?	X		
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		
7	Has the applicant submitted the results of analytical method verification studies?	X		
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?			N/A
9	If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data?			N/A, product is not intended for reconstitution or dilution.
10	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: This application is a resubmission. The subject drug product was originally part of NDA 204200, which was split, and NDA 204640 was created with a retroactive date of 07 March 2012. NDA 204640 was refused for filing by FDA on 20 September 2012 due to nonpayment of user fees. The NDA was resubmitted on 02 August 2013 and the relevant quality microbiology information (same as what was submitted for NDA

204200) was submitted on 14 August 2013. The most recent requalification studies provided are from 2011, and an information request for updated requalification data will be submitted to the applicant.

Please submit the following information request to the applicant:

1. Your application describes the use of [REDACTED] (b) (4) [REDACTED]. Provide the results of the most recent requalification studies performed [REDACTED] (b) (4).
2. Your application describes the use of [REDACTED] (b) (4) [REDACTED] vials. Provide the results of the most recent requalification studies performed [REDACTED] (b) (4).
3. Your application describes the use of [REDACTED] (b) (4) for product filling. Provide results from the most recent media fills performed on these lines.

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Erika Pfeiler, Ph.D.

Date

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John Metcalfe, Ph.D.

Date

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/s/  
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ERIKA A PFEILER  
08/21/2013

JOHN W METCALFE  
08/21/2013  
I concur.