

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**203049Orig1s000**

**MICROBIOLOGY REVIEW(S)**

# Product Quality Microbiology Review

28 November 2011

**NDA:** 203-049/N000

**Drug Product Name**

**Proprietary:** NA

**Non-proprietary:** Argatroban Injection

**Review Number:** 1

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

<b>Submit</b>	<b>Received</b>	<b>Review Request</b>	<b>Assigned to Reviewer</b>
18 March 2011	21 March 2011	30 March 2011	31 March 2011
29 September 2011 (SD 8)	20 September 2011	NA	NA
25 October 2011 (SD 12)	26 October 2011	NA	NA

**Submission History (for amendments only) - NA**

**Applicant/Sponsor**

**Name:** Hikma Pharmaceuticals Co. Ltd.

**Address:** Industrial Area  
Bayader Wadi El Seer  
Amman Jordan

**U. S. Agent:** Jonathan Sterling, Exela Pharma Sciences  
Director of Quality

**Telephone:** (828) 448-8744

**Name of Reviewer:** Denise A. Miller

**Conclusion:** Approve

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## Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** Original new drug application
  2. **SUBMISSION PROVIDES FOR:** The manufacture and (b) (4) (b) (4) of Argatroban Injection 100 mg/mL.
  3. **MANUFACTURING SITE:**  
Afton Scientific Corporation  
2030 Avon Court  
Charlottesville, Va. 22902
  4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
    - Dosage form: Sterile liquid
    - Route of Administration: Intravenous
    - Strength/Potency: 100 mg/mL
  5. **METHOD(S) OF STERILIZATION:** (b) (4)
  6. **PHARMACOLOGICAL CATEGORY:** Thrombin inhibitor
- B. **SUPPORTING/RELATED DOCUMENTS:**  
DMF (b) (4) (b) (4)
- C. **REMARKS:**
- 1) Application is electronic non-CTD format.
  - 2) The following microbiology information requests (IR) were sent during this review:
    - a) IR #1 sent on 12 August 2011; response received 30 September 2011.
    - b) IR #2 sent on 24 October 2011; response received 25 October 2011.

**filename:** N203049N000R1.doc

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## **Executive Summary**

### **I. Recommendations**

- A. Recommendation on Approvability** - Recommend to approve from a quality microbiology standpoint.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** - NA

### **II. Summary of Microbiology Assessments**

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** - This product is (b) (4)
- B. Brief Description of Microbiology Deficiencies** – There are no deficiencies based on the microbiological information provided; however, there are several comments to be forwarded to the sponsor (see page 13 section H).
- C. Assessment of Risk Due to Microbiology Deficiencies** - NA

### **III. Administrative**

- A. Reviewer's Signature** \_\_\_\_\_  
Denise A. Miller, Microbiologist, NDMS
- B. Endorsement Block** \_\_\_\_\_  
Bryan S. Riley, Senior Microbiologist
- C. CC Block**  
N/A

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/s/  
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DENISE A MILLER  
11/29/2011

BRYAN S RILEY  
11/29/2011  
I concur.

## PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

**NDA Number:** 203-049

**Applicant:** HIKMA  
Pharmaceuticals, Inc.

**Letter Date:** 18 Mar 011

**Drug Name:** Argatroban  
Injection

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

**Stamp Date:** 21 Mar 2011

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?	√		
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	√		
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	√		Hold time study (b) (4)
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?		√	
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?	√		PE is NA CC submitted
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	√		
7	Has the applicant submitted the results of analytical method verification studies?	√		Both B&F and E&I studies present
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	NA		
9	Is this NDA fileable? If not, then describe why.	√		

Denise A. Miller, Microbiologist

Date

James L. McVey, Quality Microbiology Team Leader

Date

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/s/  
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DENISE A MILLER  
05/09/2011

JAMES L MCVEY  
05/09/2011  
I concur.