APPLICATION NUMBER:

022450Orig1s000

MICROBIOLOGY REVIEW(S)
Product Quality Microbiology Review

13 OCTOBER 2009

NDA: 22-450/N000

Drug Product Name
Proprietary: Acetavance
Non-proprietary: Acetaminophen

Review Number: 1

Dates of Submission(s) Covered by this Review

<table>
<thead>
<tr>
<th>Letter Stamp</th>
<th>Review Request</th>
<th>Assigned to Reviewer</th>
</tr>
</thead>
</table>

Submission History (for amendments only) – NA

Applicant/Sponsor
Name: Cadence Pharmaceuticals
Address: 12481 High Bluff Drive, Suite 200
San Diego, CA 92130
Representative: Malcolm Lloyd-Smith
Telephone: (858) 436-1400

Conclusion: Approve
Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original submission

2. SUBMISSION PROVIDES FOR: The submission provides for the manufacture and sterilization of acetaminophen for injection.

3. MANUFACTURING SITE:
Baxter Healthcare Corporation
911 North Davis Ave.
Cleveland, MS 38732
FDA Registration Number: 1019003

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:
   - Liquid for Injection, 100 mL vials containing 100 mL
   - Intravenous
   - 10 mg/mL

5. METHOD(S) OF STERILIZATION: (b) (4)

6. PHARMACOLOGICAL CATEGORY: Treatment of pain and fever

B. SUPPORTING/RELATED DOCUMENTS:
Baxter DMF 4681 Production of Parenteral Injections in Glass Containers

C. REMARKS:
Submission is in e-CTD format.
Review of Baxter DMF 4681 concluded that the DMF was adequate to support NDA 22-450/N000. See DMF review D4681_2009OCT02_A1.doc.

filename: N022450N000R1.doc
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 – N/A

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – The manufacture and sterilization of acetaminophen injection.

B. Brief Description of Microbiology Deficiencies - None

C. Assessment of Risk Due to Microbiology Deficiencies - NA

III. Administrative

A. Reviewer's Signature _____________________________
   Denise A. Miller, Microbiologist

B. Endorsement Block ______________________________
   Bryan S. Riley, Ph. D.

C. CC Block
   N/A

5 Pages have been Withheld in Full as b4 (CCI/TS) Immediately Following this Page
<table>
<thead>
<tr>
<th>Application Type/Number</th>
<th>Submission Type/Number</th>
<th>Submitter Name</th>
<th>Product Name</th>
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</thead>
<tbody>
<tr>
<td>NDA-22450</td>
<td>ORIG-1</td>
<td>CADENCE PHARMACEUTICALS INC</td>
<td>ACETAMINOPHEN FOR INJECTION FOR IV USE</td>
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This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

DENISE A MILLER  
10/13/2009

BRYAN S RILEY  
10/13/2009  
I concur.
PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

**NDA Number:** 22-450  **Applicant:** Cadence Pharmaceuticals  **Letter Date:** 13-MAY-2009

**Drug Name:** Acetavance  **NDA Type:** 505(b)(2)  **Stamp Date:** 13-MAY-2009

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

<table>
<thead>
<tr>
<th>Content Parameter</th>
<th>Yes</th>
<th>No</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>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?</td>
<td>√</td>
<td></td>
<td>e-CDT format</td>
</tr>
<tr>
<td>2 Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?</td>
<td>√</td>
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<tr>
<td>3 Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?</td>
<td>√</td>
<td></td>
<td>(b) (4) sterilization (b) (4) reference to DMF 4681</td>
</tr>
<tr>
<td>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?</td>
<td>√</td>
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<tr>
<td>5 Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?</td>
<td>√</td>
<td></td>
<td>PE= NA CC = reference to DMF 4681</td>
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<td>6 Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?</td>
<td>√</td>
<td></td>
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<tr>
<td>7 Has the applicant submitted the results of analytical method verification studies?</td>
<td>√</td>
<td></td>
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<tr>
<td>8 Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?</td>
<td>NA</td>
<td></td>
<td></td>
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<tr>
<td>9 Is this NDA fileable? If not, then describe why.</td>
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Additional Comments: This submission is for acetaminophen to be administered I.V. without admixture. Label states that the product must be used within 6 hours of releasing vacuum in the vial and administered as a 15 minute infusion; therefore there are no post reconstitution microbial issues.

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Denise Miller, Microbiologist  Date

Bryan S. Riley, Ph.D.  Date
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/
Denise Miller
7/9/2009 09:23:27 AM
MICROBIOLOGIST

Bryan Riley
7/9/2009 09:26:36 AM
MICROBIOLOGIST
I concur.