APPLICATION NUMBER:
201517Orig1s000

MICROBIOLOGY REVIEW(S)
Product Quality Microbiology Review

10 MAY 2011

NDA: 201517

Drug Product Name
   Proprietary: N/A
   Non-proprietary: Morphine Sulfate Oral Solution

Review Number: 2

Dates of Submission(s) Covered by this Review

<table>
<thead>
<tr>
<th>Submit</th>
<th>Received</th>
<th>Review Request</th>
<th>Assigned to Reviewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>21 December 2010</td>
<td>23 December 2010</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>3 December 2010</td>
<td>7 December 2010</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Submission History (for amendments only):

<table>
<thead>
<tr>
<th>Submit Date(s)</th>
<th>Microbiology Review #</th>
<th>Review Date(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>26 February 2010</td>
<td>1</td>
<td>30 August 2010</td>
</tr>
</tbody>
</table>

Applicant/Sponsor
   Name: Lannett Holdings, Inc.
   Address: 9000 State Road, Philadelphia, PA 19136
   Representative: Ernest Sabo, VP Regulatory and Compliance
   Telephone: 215-333-9000

Name of Reviewer: Bryan S. Riley, Ph.D.

Conclusion: Recommend Approval
Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUBMISSION:** Amendments to a 505(b)(2) NDA

2. **SUBMISSION PROVIDES FOR:** A new drug product

3. **MANUFACTURING SITE:** Cody Laboratories
   601 Yellowstone Ave

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** (b)(4), preserved aqueous solution for oral administration

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

6. **PHARMACOLOGICAL CATEGORY:** Opioid Analgesic

B. **SUPPORTING/RELATED DOCUMENTS:** N/A

C. **REMARKS:** This was an eCTD submission. A product quality microbiology deficiency was sent to the applicant in a Discipline Review Letter dated 8 September 2010. The deficiency concerned the lack of a specification for the absence of *Burkholderia cepacia* in the drug product. The applicant responded in amendments dated 3 and 21 December 2010.

*filename:* N201517R1.doc
Executive Summary

I. Recommendations

A. Recommendation on Approvability – This submission is recommended for approval on the basis of product quality microbiology.

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 drug product is a preserved aqueous solution. The applicant has added a test method for the presence of *Burkholderia cepacia*.

B. Brief Description of Microbiology Deficiencies – N/A

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

III. Administrative

A. Reviewer's Signature _____________________________
   Bryan S. Riley, Ph.D.
   Senior Review Microbiologist, OPS/NDMS

B. Endorsement Block _____________________________
   Stephen E. Langille, Ph.D.
   Senior Review Microbiologist, OPS/NDMS

C. CC Block
   N/A
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

BRYAN S RILEY
05/10/2011

STEPHEN E LANGILLE
05/10/2011
Product Quality Microbiology Review

30 AUGUST 2010

NDA: 201517

Drug Product Name
Proprietary: N/A
Non-proprietary: Morphine Sulfate Oral Solution

Review Number: 1

Dates of Submission(s) Covered by this Review

<table>
<thead>
<tr>
<th>Submit</th>
<th>Received</th>
<th>Review Request</th>
<th>Assigned to Reviewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>26 February 2010</td>
<td>1 March 2010</td>
<td>14 July 2010</td>
<td>15 July 2010</td>
</tr>
</tbody>
</table>

Submission History (for amendments only): N/A

Applicant/Sponsor
Name: Lannett Holdings, Inc.
Address: 9000 State Road, Philadelphia, PA 19136
Representative: Ernest Sabo, VP Regulatory and Compliance
Telephone: 215-333-9000

Name of Reviewer: Bryan S. Riley, Ph.D.

Conclusion: Approvable pending resolution of product quality microbiology deficiencies. Please see “List of Product Quality Microbiology Deficiencies” at the end of this review.
Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: 505(b)(2) NDA

2. SUBMISSION PROVIDES FOR: A new drug product

3. MANUFACTURING SITE: Cody Laboratories
   601 Yellowstone Ave

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: preserved aqueous solution for oral administration

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

6. PHARMACOLOGICAL CATEGORY: Opioid Analgesic

B. SUPPORTING/RELATED DOCUMENTS: N/A

C. REMARKS: This was an eCTD submission. The consult request asked for a review of the preservative effectiveness testing.

filename: N201517R1.doc
Executive Summary

I. Recommendations

A. Recommendation on Approvability – This submission is approvable pending resolution of a product quality microbiology deficiency. Please see “List of Product Quality Microbiology Deficiencies” at the end of this review.

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 drug product is a preserved aqueous solution.

B. Brief Description of Microbiology Deficiencies - The drug product manufacturing process does not provide for control of *Burkholderia cepacia*.

C. Assessment of Risk Due to Microbiology Deficiencies – *Burkholderia cepacia* is a potential human pathogen which is often resistant to antimicrobial preservatives. Preservative-resistant *B. cepacia* could proliferate in the drug product and cause disease in the patient.

III. Administrative

A. Reviewer's Signature _____________________________
   Bryan S. Riley, Ph.D.
   Senior Review Microbiologist, OPS/NDMS

B. Endorsement Block _____________________________
   Stephen E. Langille, Ph.D.
   Senior Review Microbiologist, OPS/NDMS

C. CC Block
   N/A

2 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>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>NDA-201517</td>
<td>ORIG-1</td>
<td>LANNETT HOLDINGS INC</td>
<td>morphine sulfate oral solution 20 mg/mL</td>
<td></td>
</tr>
</tbody>
</table>

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

BRYAN S RILEY
08/31/2010

STEPHEN E LANGILLE
09/01/2010