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RESEARCH**

APPLICATION NUMBER:
200535Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

14 OCTOBER 2010

NDA: 200-535/SD-14, -18 -19

Drug Product Name

Proprietary: None

Non-proprietary: Oxycodone hydrochloride oral solution

Review Number: 2

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
28 September 2010	28 September 2010	28 September 2010	28 September 2010
01 October 2010	04 October 2010	na	na
07 October 2010	07 October 2010	na	na

Submission History (for amendments only):

Submit Date(s)	Microbiology Review #	Review Date(s)
22 December 2009	1	22 September 2010

Applicant/Sponsor

Name: Lehigh Valley Technologies, Inc.

Address: 514 N. 12th Street
Allentown, PA 18102

Representative: William Reightler
Director, QA/Regulatory Affairs

Telephone: 610-782-9780 x18

Name of Reviewer: Robert J. Mello, Ph.D.

Conclusion: Recommend Approval

Product Quality Microbiology Data Sheet

- A.**
- 1. TYPE OF SUBMISSION:** 505(b)(2) NDA
 - 2. SUBMISSION PROVIDES FOR:** Marketing Authorization
 - 3. MANUFACTURING SITE:** Lehigh Valley Technologies, Inc.
514 N. 12th Street
Allentown, PA 18102
 - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Non-sterile, (b) (4) aqueous solution for oral administration, (b) (4) 20mg/ml.
 - 5. METHOD(S) OF STERILIZATION:** Not Applicable
 - 6. PHARMACOLOGICAL CATEGORY:** Opioid Analgesic
- B. SUPPORTING/RELATED DOCUMENTS:** None
- C. REMARKS:**
- This is an eCTD submission. The original PDUFA date is 22 October 2010.
 - An Information Request was submitted by the Division on 23 September 2010 containing both chemistry and microbiology questions. The Microbiology issues raised in Microbiology Review #1 concerned batch identification codes used in the (b) (4), a lack of microbial limits testing and a lack of control for *B. cepacia*. The Applicant's responses of 28 September 2010 (DARRTS Supporting Document 14) and 01 October 2010 (DARRTS Supporting Document 18) were acceptable in part except that the specification for total combined yeast and mold remained unacceptably high. An additional Information Request was transmitted on 06 October 2010. The Applicant responded on 07 October 2010 (DARRTS Supporting Document 19).

filename: N200535N000R2.doc

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 – The drug product is a non-sterile (b) (4) aqueous solution.**
- B. Brief Description of Microbiology Deficiencies – None**
- C. Assessment of Risk Due to Microbiology Deficiencies – N/A**

III. Administrative

- A. Reviewer's Signature:** _____
Robert J. Mello, Ph.D.
Senior Microbiology Reviewer
- B. Endorsement Block:** _____
John W. Metcalfe, Ph.D.
Senior Microbiology Reviewer
- C. CC Block**
NDA 200535 file

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/s/

ROBERT J MELLO
10/14/2010

JOHN W METCALFE
10/14/2010
I concur.

Product Quality Microbiology Review

22 SEPTEMBER 2010

NDA: 200-535

Drug Product Name

Proprietary: None

Non-proprietary: Oxycodone hydrochloride oral solution

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
22 December 2009	22 December 2009	29 September 2010	20 September 2010
19 August 2010	20 August 2010	na	na

Submission History (for amendments only): NA

Applicant/Sponsor

Name: Lehigh Valley Technologies, Inc.

Address: 514 N. 12th Street
Allentown, PA 18102

Representative: William Reightler
Director, QA/Regulatory Affairs

Telephone: 610-782-9780 x18

Name of Reviewer: Robert J. Mello, Ph.D.

Conclusion: Approvable pending resolution of product quality microbiology deficiencies. (See Section 3 “List of Product Quality Microbiology Deficiencies”)

Product Quality Microbiology Data Sheet

- A.**
- 1. TYPE OF SUBMISSION:** 505(b)(2) NDA
 - 2. SUBMISSION PROVIDES FOR:** Marketing Authorization
 - 3. MANUFACTURING SITE:** Lehigh Valley Technologies, Inc.
514 N. 12th Street
Allentown, PA 18102
 - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Non-sterile, (b) (4) aqueous solution for oral administration, (b) (4) 20mg/ml.
 - 5. METHOD(S) OF STERILIZATION:** Not Applicable
 - 6. PHARMACOLOGICAL CATEGORY:** Opioid Analgesic
- B. SUPPORTING/RELATED DOCUMENTS:** None
- C. REMARKS:**
- This is an eCTD submission. The consult request asked for a review of the (b) (4). The August 19, 2010 amendment contained the latest version of the drug product specifications.

filename: N200535N000R1.doc

Executive Summary

I. Recommendations

- A. Recommendation on Approvability** - This submission is approvable pending resolution of product quality microbiology deficiencies. Please see Section 3, "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 non-sterile (b) (4) aqueous solution.
- B. Brief Description of Microbiology Deficiencies** – The drug product lacks a specification for microbial limits. Also, the drug product manufacturing process does not provide for control of *Burkholderia cepacia*.
- C. Assessment of Risk Due to Microbiology Deficiencies** - Microbial limits testing of the drug product confirms a minimum degree of microbial control over the manufacturing process. Non-sterile drug products must also be free of objectionable organisms. *Burkholderia cepacia* is a potential human pathogen (b) (4) *B. cepacia* could proliferate in the drug product and cause disease in the patient.

III. Administrative

- A. Reviewer's Signature:** _____
Robert J. Mello, Ph.D.
Senior Microbiology Reviewer
- B. Endorsement Block:** _____
John W. Metcalfe, Ph.D.
Senior Microbiology Reviewer
- C. CC Block**
NDA 200535 file

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/s/

ROBERT J MELLO
09/22/2010

JOHN W METCALFE
09/22/2010
I concur.