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RESEARCH**

APPLICATION NUMBER:
022234Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

10 DECEMBER 2009

NDA: 22-234

Drug Product Name

Proprietary: N/A

Non-proprietary: Docetaxel Injection

Review Number: 3

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
12 June 2009	12 June 2009	23 November 2009	24 November 2009

Submission History (for amendments only)

Submit Date(s)	Microbiology Review #	Review Date(s)
9 July 2007	1	11 April 2008
24 April 2008	2	6 June 2008

Applicant/Sponsor

Name: Hospira, Inc.

Address: 275 North Field Dr., Dept 0389, Bldg. H2-2, Lake Forest, IL 60045

Representative: Wendy Tian

Telephone: 224-212-6163

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

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

- A.
- 1. TYPE OF SUBMISSION:** Amendment to Pending Application
 - 2. SUBMISSION PROVIDES FOR:** A Parenteral Drug Product
 - 3. MANUFACTURING SITE:**

Zydu Hospira Oncology Private Ltd. (ZHOPL)
Pharmez
Special Economic Zone Plot No. 3
Matoda
Sarkhej Bavla Highway
Taluka Sanand
District Ahmedabad-382 210
Gujarat, India
 - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Sterile non-aqueous solution in glass vials, 2 mL in 2 mL vial, 8 mL in 10 mL vial and 16 mL in 20 mL vial for intravenous administration, 10 mg/mL.
 - 5. METHOD(S) OF STERILIZATION:** (b) (4)
 - 6. PHARMACOLOGICAL CATEGORY:** Cytotoxic Drug
- B. **SUPPORTING/RELATED DOCUMENTS:** Product Quality Microbiology review of Type V DMF (b) (4).
- C. **REMARKS:** This was an eCTD submission. This amendment was submitted to add an alternate manufacturing facility to (b) (4) for the drug product. The original NDA was tentatively approved due to patent issues.

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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 (b) (4) [REDACTED].
- 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.
- B. Endorsement Block** _____
James L. McVey, NDMS Team Leader
- C. CC Block**
N/A

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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22234	ORIG-1	HOSPIRA INC	DOCETAXEL INJECTION

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/s/

BRYAN S RILEY
12/10/2009

JAMES L MCVEY
12/10/2009
I concur.

Product Quality Microbiology Review

06 JUN 2008

NDA: 22-234 AC

Drug Product Name

Proprietary: N/A
Non-proprietary: Docetaxel Injection
Drug Product Priority Classification: 5S

Review Number: 2

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
24-APR-2008	28-APR-2008	25-APR-2008	28-APR-2008

Submission History (for amendments only)

Submission Date(s)	Microbiology Review #	Review Date(s)
09-JUL-2007	1	11-APR-2008

Applicant/Sponsor

Name: Hospira, Inc.
Address: 275 N. Field Dr.
Lake Forest, IL 60045-5046

Representative: Judith Zutkis
Director, Global Regulatory Affairs
Telephone: 224-212-4949
E-mail: judith.zutkis@secure.hospira.com

Name of Reviewer: Anastasia G. Lolas

Conclusion: Recommended for approval

Product Quality Microbiology Data Sheet

- A.**
- 1. TYPE OF SUBMISSION:** Amendment to new drug application
 - 2. SUBMISSION PROVIDES FOR:** Response to microbiology questions sent on 11-APR-2008
 - 3. MANUFACTURING SITE:** Mayne Pharma Limited
1 Lexia Place, Mulgrave
Victoria 3170
Australia
 - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - Sterile non-aqueous solution in glass vials: 2 mL/2 mL fill, 10 mL/8 mL fill and 20 mL/16 mL fill
 - Intravenous administration
 - 10 mg/mL
 - 5. METHOD(S) OF STERILIZATION:** (b) (4)
 - 6. PHARMACOLOGICAL CATEGORY:** Cytotoxic drugs
- B. SUPPORTING/RELATED DOCUMENTS:**
- NDA 20-449
 - Microbiology Review #1 of NDA 22-234 dated 11-APR-2008
- C. REMARKS:** The first microbiology review identified 6 questions to be sent to the applicant. An electronic communication was sent on 11-APR-2008. An electronic response was received on 25-APR-2008.

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Executive Summary

I. Recommendations

- A. Recommendation on Approvability** – NDA 22-234 is recommended for approval based on 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 product is (b) (4) into single-dose and multiple-dose glass vials.
- B. Brief Description of Microbiology Deficiencies** – None
- C. Assessment of Risk Due to Microbiology Deficiencies** – N/A

III. Administrative

- A. Reviewer's Signature** _____
Anastasia G. Lolas
- B. Endorsement Block**
Bryan S. Riley, Ph.D.
- C. CC Block**
N/A

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/s/

Anastasia Lolas
6/6/2008 02:48:39 PM
MICROBIOLOGIST

Bryan Riley
6/9/2008 07:35:27 AM
MICROBIOLOGIST
I concur.

Product Quality Microbiology Review

11 APR 2008

NDA: 22-234

Drug Product Name

Proprietary: N/A
Non-proprietary: Docetaxel Injection
Drug Product Priority Classification: 5S

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
09-JUL-2007	11-JUL-2007	22-AUG-2007	23-AUG-2007

Submission History (for amendments only) – N/A

Applicant/Sponsor

Name: Hospira, Inc.
Address: 275 N. Field Dr.
Lake Forest, IL 60045-5046

Representative: Mary Pontikes
Sr. Associate, Global Regulatory Affairs

Telephone: 224-212-4852

E-mail: mary.pontikes@secure.hospira.com

Name of Reviewer: Anastasia G. Lolas

Conclusion: Approvable pending the resolution of product quality microbiology deficiencies (see Section 3 of review)

Product Quality Microbiology Data Sheet

- A.
- 1. TYPE OF SUBMISSION:** Original new drug application
 - 2. SUBMISSION PROVIDES FOR:** New drug product based on an already marketed product
 - 3. MANUFACTURING SITE:** Mayne Pharma Limited
1 Lexia Place, Mulgrave
Victoria 3170
Australia
 - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - Sterile non-aqueous solution in glass vials: 2 mL/2 mL fill, 10 mL/8 mL fill and 20 mL/16 mL fill
 - Intravenous administration
 - 10 mg/mL
 - 5. METHOD(S) OF STERILIZATION:** (b) (4)
 - 6. PHARMACOLOGICAL CATEGORY:** Cytotoxic drugs
- B. **SUPPORTING/RELATED DOCUMENTS:** NDA 20-449
- C. **REMARKS:** This is a 505(b)(2) application submitted in paper and in CTD format. A copy of Modules 1 and 2 (one volume each) and Module 3, Volumes 1.1-1.6 were provided for review. The reference drug is TAXOTERE® (NDA 20-449). Compared to the reference drug, the proposed product has a slightly different formulation that allows a multi-dose presentation. In addition, it can be directly diluted in normal saline or dextrose solution and then infused, while TAXOTERE® requires two steps: firstly dilution with a diluent and then further dilution in normal saline or dextrose solution prior to infusion.

The Initial Quality Assessment has identified product quality microbiology as a critical issue in the review of this application. In addition, the applicant has submitted a (b) (4).

file name: N022234R1.doc

Executive Summary

I. Recommendations

- A. Recommendation on Approvability** – NDA 22-234 is approvable pending the resolution of product quality microbiology deficiencies (see Section 3)
- 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 product is [REDACTED] (b) (4) into single-dose and multiple-dose glass vials.
- B. Brief Description of Microbiology Deficiencies** – The applicant has not provided detailed enough information regarding the validation of depyrogenation/sterilization processes. The [REDACTED] (b) (4) does not follow the draft guidance and lacks sufficient detail.
- C. Assessment of Risk Due to Microbiology Deficiencies** – Moderate risk. It is difficult to assess the results of some of the studies without adequate information on the protocols followed.

III. Administrative

- A. Reviewer's Signature** _____
Anastasia G. Lolas
- B. Endorsement Block**
Bryan S. Riley, Ph.D.
- C. CC Block**
N/A

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/s/

Anastasia Lolas
4/11/2008 11:04:16 AM
MICROBIOLOGIST

Bryan Riley
4/11/2008 11:09:45 AM
MICROBIOLOGIST