CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

200795Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

5 July 2011

NDA: **200-795**

Drug Product Name
Proprietary: Not applicable
Non-proprietary: Gemcitabine Injection

Review Number: 2

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
10 June 2011	10 June 2011	14 June 2011	15 June 2011

Submission History (for amendments only): Not applicable

Submit	Received	Review Request	Assigned to Reviewer
11 December 2009	11 December 2009	13 January 2010	14 January 2010
9 September 2010	9 September 2010	N/A	N/A

Applicant/Sponsor
Name: Hospira Inc.
Address: 275 N. Field Drive
Dept: 0389, Bldg. H2-2
Lake Forest, IL 60045-5046

Representative: Khaled M. Mohamed
Telephone: 224-212-4909

Name of Reviewer: Stephen E. Langille, Ph.D.

Conclusion: Recommended for approval

Product Quality Microbiology Data Sheet

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

2. SUBMISSION PROVIDES FOR: [redacted] (b) (4)

3. MANUFACTURING SITE: Hospira, Inc.
1 Lexia Place
Mulgrave
Victoria 3170
Australia

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:

- Sterile solution
- Injection
- 200 mg/5.3 mL, 1 g/26.3 mL, 2 g/52.6 mL.

5. METHOD(S) OF STERILIZATION: [redacted] (b) (4)

6. PHARMACOLOGICAL CATEGORY: Treatment for breast, lung and pancreatic cancer.

B. SUPPORTING/RELATED DOCUMENTS: NDA 20-509 (Gemzar®)

C. REMARKS: The document was provided in eCTD format. The first review of NDA 200-795 was completed on 10 September 2010. A Class 1 resubmission was received on 10 June 2011.

filename: N200795r1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability -

NDA 200-795 is recommended for approval from the standpoint of product quality microbiology.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -

Not applicable

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -

The drug product will be (b) (4) processed at the Mulgrave, Victoria, Australia manufacturing site.

B. Brief Description of Microbiology Deficiencies -

No microbiology deficiencies were identified based upon the information provided.

C. Assessment of Risk Due to Microbiology Deficiencies -

Not applicable

III. Administrative

A. Reviewer's Signature _____

Stephen E. Langille

B. Endorsement Block

James McVey - Team Leader

C. CC Block

N/A

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/s/

STEPHEN E LANGILLE
07/05/2011

JAMES L MCVEY
07/08/2011
I concur.

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 22 November 2010

TO: Amy Tilley – Regulatory Project Manager
OND/OODP/DDOP

FROM: Stephen E. Langille, Ph.D.
Senior Product Quality Microbiology Reviewer
New Drug Microbiology Staff

THROUGH: James McVey
Team Leader
New Drug Microbiology Staff

SUBJECT: NDA 200-795

Microbiological studies in support of the 24 hour post-dilution/penetration storage time for Gemcitibine Injection (as stated in the proposed labeling) have not been provided. Please provide a risk assessment summarizing studies that show adventitious microbial contamination does not grow under the storage conditions proposed. In lieu of these data, the product labeling should recommend that the post-constitution storage period is not more than 4 hours at room temperature or 24 hours if refrigerated. Reference is made to *Guidance for Industry: ICH Q8 Pharmaceutical Development*, Section II.E and *Guidance for Industry*: *ICH Q1A(R2) Stability Testing of New Drug Substances and Products*, Section 2.2.7.

The report should describe test methods and results that employ a minimum countable inoculum to simulate potential microbial contamination that may occur during product dilution. The time point at which the initiation of growth is clearly evident should be identified. Sufficient replicates should be done to be able to identify when the titer is rising above the testing error of the no growth points. It is generally accepted that growth is evident when the population increases more than 0.5 Log_{10}. The test should be run at the label's recommended storage conditions and be conducted for 2 to 3-times the label's recommended storage period and using the label-recommended fluids. Periodic intermediate sample times are recommended. Challenge organisms may include strains described in USP <51> plus typical skin flora or species associated with hospital-borne infections.

END

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/s/

STEPHEN E LANGILLE
11/29/2010

JAMES L MCVEY
12/02/2010
I concur.

Product Quality Microbiology Review

10 September 2010

NDA: **200-795**

Drug Product Name
Proprietary: Not applicable
Non-proprietary: Gemcitabine Injection

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
11 December 2009	11 December 2009	13 January 2010	14 January 2010
9 September 2010	9 September 2010	N/A	N/A

Submission History (for amendments only): Not applicable

Applicant/Sponsor
Name: Hospira Inc.
Address: 275 N. Field Drive
Dept: 0389, Bldg. H2-2
Lake Forest, IL 60045-5046

Representative: Khaled M. Mohamed
Telephone: 224-212-4909

Name of Reviewer: Stephen E. Langille, Ph.D.

Conclusion: Recommended for approval

Product Quality Microbiology Data Sheet

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

2. SUBMISSION PROVIDES FOR: [redacted] (b) (4)

3. MANUFACTURING SITE: Hospira, Inc.
1 Lexia Place
Mulgrave
Victoria 3170
Australia

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:

- Sterile solution
- Injection
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5. METHOD(S) OF STERILIZATION: [redacted] (b) (4)

6. PHARMACOLOGICAL CATEGORY: Treatment for breast, lung and pancreatic cancer.

B. SUPPORTING/RELATED DOCUMENTS: NDA 20-509 (Gemzar®)

C. REMARKS: The document was provided in eCTD format.

filename: N200795r1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability -

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B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -

Not applicable

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -

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B. Brief Description of Microbiology Deficiencies -

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C. Assessment of Risk Due to Microbiology Deficiencies -

Not applicable

III. Administrative

A. Reviewer's Signature _____

Stephen E. Langille

B. Endorsement Block

James McVey - Team Leader

C. CC Block

N/A

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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

STEPHEN E LANGILLE
09/13/2010

JAMES L MCVEY
09/14/2010
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 200-795 **Applicant:** Hospira **Letter Date:** 11-December-2009

Drug Name: Gemcitabine Injection **NDA Type:** Standard **Stamp Date:** 11-December-2009

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?	X		
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		
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?		X	
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?	X		
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		
7	Has the applicant submitted the results of analytical method verification studies?	X		
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	X		No special/critical studies/data were requested with regard to sterility assurance.
9	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: The drug product is an injectable solution for the treatment of metastatic breast cancer. It will be supplied in 200 mg/5.3 mL, 1 g/26.3 mL and 2 g/52.6 mL presentations. The package insert and label were not available for review at the time of filing.

Stephen E. Langille,
Reviewing Microbiologist Date

James McVey
Microbiology Secondary Reviewer/Team Leader Date

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

STEPHEN E LANGILLE
02/09/2010
Filing review - fileable for CMC microbiology

JAMES L MCVEY
02/10/2010
I concur.