CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022312Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

21 November 2011

NDA: 22-312

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

Review Number: 4

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
27 January 2011	26 APRIL 2010	3 August 2011	4 August 2010
12 July 2011	12 July 2011	3 August 2010	4 July 2010

Submission History (for amendments only)

Submit Date(s)	Microbiology Review #	Review Date(s)
27 MARCH 2008	1	20 MARCH 2009
12 MARCH 2009	1	20 MARCH 2009
29 JULY 2009	2	10 JANUARY 2010
23 APRIL 2010	3	1 SEPTEMBER 2010
23 JULY 2010	3	1 SEPTEMBER 2010
12 AUGUST 2010	3	1 SEPTEMBER 2010
31 AUGUST 2010	3	1 SEPTEMBER 2010
24 November 2009	4	17 SEPTEMBER 2010

Name: Apotex, Inc.
Address: 150 Signet Drive,
Toronto, Ontario, Canada

Representative: Kirin Krishnan
Associate Director, Regulatory Affairs US

Telephone: (954) 384-3986

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

Conclusion: Recommended for approval

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Class 2 resubmission

2. SUBMISSION PROVIDES FOR: Responses to the CR letter issued on 4 May 2011.

3. MANUFACTURING SITE:

Apotex Inc.
380 Elgin Mills Road East
Richmond Hill, Ontario
Canada L4C 5H2

and

Apotex Inc.
Special Products Facility
285 Garyray Dr.
Weston, Ontario
Canada M9L 1P3

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

- Sterile solution for injection
- Intravenous
- 40 mg/mL

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

6. PHARMACOLOGICAL CATEGORY: Cancer therapy

B. SUPPORTING/RELATED DOCUMENTS: Product quality microbiology reviews 1, 2, 3 and 4 for NDA 22-312 completed on 20 March 2009, 10 January 2010, 1 September 2010 and 17 September 2010.

C. **REMARKS:** The submission was provided in eCTD format. Previous product quality microbiology reviews have covered the manufacture of the diluent at the Richmond Hill, Ontario site and the concentrate on the (b) (4) at the Weston, Ontario Site. The current application provides for (b) (4).

filename: N022312R4.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability -

NDA 22-312 is recommended for approval from the standpoint 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 applicant has provided a resubmission of NDA 22-312 to support changes to the (b) (4) and process for docetaxel concentrate at the Weston, Ontario manufacturing facility.

B. Brief Description of Microbiology Deficiencies -

No deficiencies have been 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, Ph.D.

B. Endorsement Block _____

Bryan Riley, Ph.D.
Senior Microbiology Reviewer

C. CC Block

N/A

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/s/

STEPHEN E LANGILLE
11/30/2011

BRYAN S RILEY
12/01/2011
I concur.

REV-QUALITYMICRO-02 (Review Noted (NAI))
NDA-022312
ORIG-1
Supporting Document 16
Patent & Exclusivity/Exclusivity Information
Resubmission/Class 2
Submit Date: 03/24/2010 - FDA Received Date: 03/24/2010

The 24 March 2010 amendment to NDA 22-312 contains [redacted] (b) (4) [redacted] On 31 August 2010, the applicant provided an amendment to NDA 22-312 withdrawing the [redacted] (b) (4) [redacted]

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/s/

STEPHEN E LANGILLE
09/22/2010

Product Quality Microbiology Review

17 SEPTEMBER 2010

NDA: 22-312

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

Review Number: 4

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
24 NOVEMBER 2009	24 NOVEMBER 2009	13 SEPTEMBER 2010	14 SEPTEMBER 2010

Submission History (for amendments only)

Submit Date(s)	Microbiology Review #	Review Date(s)
27 MARCH 2008	1	20 MARCH 2009
12 MARCH 2009	1	20 MARCH 2009
29 JULY 2009	2	10 JANUARY 2010
23 APRIL 2010	3	1 SEPTEMBER 2010
23 JULY 2010	3	1 SEPTEMBER 2010
12 AUGUST 2010	3	1 SEPTEMBER 2010
31 AUGUST 2010	3	1 SEPTEMBER 2010

Name: Apotex, Inc.
Address: 150 Signet Drive,
Toronto, Ontario, Canada

Representative: Kirin Krishnan
Associate Director, Regulatory Affairs US

Telephone: (954) 384-3986

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

Conclusion: Recommended for approval

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: NDA amendment

2. SUBMISSION PROVIDES FOR: (b) (4) for the drug product diluent at the Richmond Hills manufacturing facility.

3. MANUFACTURING SITE: Apotex Inc.
380 Elgin Mills Road East
Richmond Hill, Ontario
Canada L4C 5H2

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

- Sterile solution for injection
- Intravenous
- 40 mg/mL

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

6. PHARMACOLOGICAL CATEGORY: Cancer therapy

B. SUPPORTING/RELATED DOCUMENTS: Three previous product quality microbiology reviews of NDA 22-312 were completed on 20 March 2009, 10 January 2010, and 1 September 2010.

C. REMARKS: NDA 22-312 was recommended for approval for product quality microbiology on 1 September 2010. However, that review did not cover the (b) (4) change for the drug product diluent provided in the 24 November 2009 amendment. This review covers the proposed use of the (b) (4) at the Apotex Richmond Hills facility for (b) (4) docetaxel injection diluent.

filename: N022312R4.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability -
NDA 22-312 is recommended for approval from the standpoint 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 applicant proposes the use of the [redacted] (b) (4) at the Richmond Hills manufacturing facility for [redacted] (b) (4) docetaxel injection diluent.

B. Brief Description of Microbiology Deficiencies -
No 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, Ph.D.
Senior Microbiology Reviewer
Office of Pharmaceutical Science

B. Endorsement Block _____
Bryan Riley, Ph.D.
Senior Microbiology Reviewer
Office of Pharmaceutical Science

C. CC Block
N/A

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/s/

STEPHEN E LANGILLE
09/17/2010

BRYAN S RILEY
09/17/2010
I concur.

Product Quality Microbiology Review

1 SEPTEMBER 2010

NDA: 22-312

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

Review Number: 3

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
23 APRIL 2010	26 APRIL 2010	20 APRIL 2010	22 APRIL 2010
23 JULY 2010	23 JULY 2010	N/A	N/A
12 AUGUST 2010	12 AUGUST 2010	N/A	N/A
31 AUGUST 2010	31 AUGUST 2010	N/A	N/A

Submission History (for amendments only)

Submit Date(s)	Microbiology Review #	Review Date(s)
27 MARCH 2008	1	20 MARCH 2009
12 MARCH 2009	1	20 MARCH 2009
29 JULY 2009	2	10 JANUARY 2010

Name: Apotex, Inc.
Address: 150 Signet Drive,
Toronto, Ontario, Canada

Representative: Kirin Krishnan
Associate Director, Regulatory Affairs US

Telephone: (954) 384-3986

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

Conclusion: Recommended for approval

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: NDA amendment

2. SUBMISSION PROVIDES FOR: Responses to the CR letter issued on 29-January-2010 regarding a (b) (4) protocol (b) (4)

3. MANUFACTURING SITE:

Apotex Inc.
380 Elgin Mills Road East
Richmond Hill, Ontario
Canada L4C 5H2

and

Apotex Inc.
Special Products Facility
285 Garyray Dr.
Weston, Ontario
Canada M9L 1P3

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

- Sterile solution for injection
- Intravenous
- 40 mg/mL

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

6. PHARMACOLOGICAL CATEGORY: Cancer therapy

B. SUPPORTING/RELATED DOCUMENTS: Product quality microbiology review #1 for NDA 22-312 completed on 20 March 2009.

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

filename: N022312R3.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability -
NDA 22-312 is recommended for approval from the standpoint 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 applicant has withdrawn a (b) (4) protocol (b) (4)

B. Brief Description of Microbiology Deficiencies -
No 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, Ph.D.

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-22312	ORIG-1		DOCETAXEL INJECTION 40 MG ML

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/s/

STEPHEN E LANGILLE
09/01/2010

JAMES L MCVEY
09/01/2010
I concur.

Product Quality Microbiology Review

8-JANUARY-2010

NDA: 22-312

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

Review Number: 2

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
29-JULY-2009	29-JULY-2009	2-SEPTEMBER-2009	3-SEPTEMBER-2009

Submission History (for amendments only)

Submit Date(s)	Microbiology Review #	Review Date(s)
27-MARCH-2008	1	20-MARCH-2009
12-MARCH-2009	1	20-MARCH-2009

Name: Apotex, Inc.
Address: 150 Signet Drive,
Toronto, Ontario, Canada

Representative: Kirin Krishnan
Associate Director, Regulatory Affairs US

Telephone: (954) 384-3986

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

Conclusion: Approvable pending revision

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: NDA amendment

2. SUBMISSION PROVIDES FOR: Responses to the CR letter issued on 28-APRIL-2009 and a (b) (4) protocol (b) (4)

3. MANUFACTURING SITE: Apotex Inc.
380 Elgin Mills Road East
Richmond Hill, Ontario
Canada L4C 5H2

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

- Sterile solution for injection
- Intravenous
- 40 mg/mL

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

6. PHARMACOLOGICAL CATEGORY: Cancer therapy

B. SUPPORTING/RELATED DOCUMENTS: Product quality microbiology review #1 for NDA 22-312.

C. REMARKS: The first product quality microbiology review of NDA 22-312 was completed on 20-MARCH-2009 and recommended for approval from the standpoint of product quality microbiology. A Complete Response (CR) letter was sent to the applicant on 28-APRIL-2009. The 29-JULY-2009 response to the CR letter contained a (b) (4) protocol (b) (4) that is the subject of this review.

filename: N022312R2.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability -

NDA 22-312 is approvable pending the resolution of product quality microbiology deficiencies.

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 applicant has submitted a (b) (4) protocol (b) (4)

B. Brief Description of Microbiology Deficiencies -

The (b) (4) protocol does not contain sufficient information to support the proposed (b) (4)

C. Assessment of Risk Due to Microbiology Deficiencies -

Failure to address the microbiology deficiencies could result in microbial and/or endotoxin contamination of the drug product.

III. Administrative

A. Reviewer's Signature _____

Stephen E. Langille

B. Endorsement Block

James McVey – Team Leader

C. CC Block

N/A

6 Page(s) have been Withheld in Full as b4 (CCI/TS) immediately following this page

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22312	ORIG-1		DOCETAXEL INJECTION 40 MG ML

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/s/

STEPHEN E LANGILLE
01/11/2010

JAMES L MCVEY
01/12/2010
I concur.

Product Quality Microbiology Review

20-MARCH-2009

NDA: 22-312/N-000
22-312/N-000-BZ
22-312/N-000-BI

Drug Product Name
Proprietary: Not applicable
Non-proprietary: Docetaxel Injection
Drug Product Priority Classification: Standard

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
3/27/08	3/28/08	5/24/08	10/9/08
3/12/09	3/12/09	N/A	N/A

Submission History (for amendments only): Not applicable

Applicant/Sponsor
Name: Apotex, Inc.
Address: 150 Signet Drive,
Toronto, Ontario, Canada

Representative: Bernice Tao
Director, Regulatory Affairs US

Telephone: (416) 401-7889

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

Conclusion: Recommended for approval

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original NDA

2. SUBMISSION PROVIDES FOR: Sterility assurance information for the sterile concentrated drug product and the sterile diluent.

3. MANUFACTURING SITES:
Docetaxel Injection will be manufactured at

Apotex Inc. – Special Products Facility
285 Garyray Drive
Weston, Ontario
Canada M9L1P3

Docetaxel Diluent, Injection will be manufactured at

Apotex Inc.
380 Elgin Mills Road East
Richmond Hill, Ontario
Canada L4C 5H2

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

- Sterile solution for injection
- Intravenous
- 40 mg/mL

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

6. PHARMACOLOGICAL CATEGORY: Cancer therapy

B. SUPPORTING/RELATED DOCUMENTS: Not applicable

C. REMARKS: The application was submitted in eCTD format. An initial quality assessment was entered into DFS on May 21, 2008. Product quality microbiology information requests were sent to the applicant on December 12, 2008 and February 12, 2009. Responses to the information requests were provided on March 12, 2009.

filename: N022312R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability -

NDA 22-312 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 -

Taxotere for Injection will be supplied in the form of a kit containing a drug concentrate and an accompanying diluent. Each will be (b) (4)

B. Brief Description of Microbiology Deficiencies -

No 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, Ph.D.

B. Endorsement Block

James McVey – Team Leader

C. CC Block

N/A

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/s/

Stephen Langille
3/24/2009 10:39:22 AM
MICROBIOLOGIST

James McVey
3/24/2009 01:07:40 PM
MICROBIOLOGIST
I concur.