CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

203341Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

11 June 2012

NDA: **203-341/N-000**

Drug Product Name
Proprietary: Bosulif®
Non-proprietary: bosutinib monohydrate

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
17 November 2011	17 November 2011	12 December 2011	15 December 2012
06 March 2012	06 March 2012	n/a	n/a
16 May 2012	16 May 2012	n/a	n/a
31 May 2012	31 May 2012	n/a	n/a

Submission History (for amendments only): N/A

Applicant/Sponsor
Name: Wyeth Pharmaceutical, Inc.
(Wholly owned subsidiary of Pfizer, Inc.)
Address: 500 Arcola Rd.
Collegeville, PA 19426-3982
Representative: Carl M. DeJuliis, Pharm. D.
Telephone: 860-441-1693

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

Conclusion: The application is recommended for approval from microbiology product quality standpoint.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: New Drug Application

2. SUBMISSION PROVIDES FOR: Marketing Authorization

3. MANUFACTURING SITE: (b) (4)

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Film coated tablets; oral administration; 100 mg and 500 mg. Packaging is in 60ml HDPE bottles with a 28mm screw cap closure and an inner aluminum foil/ (b) (4). A single HDPE silica gel desiccant canister is included in each container.

5. METHOD(S) OF STERILIZATION: N/A. The drug product is a non-sterile tablet.

6. PHARMACOLOGICAL CATEGORY: Tyrosine kinase inhibitor for the treatment of chronic, accelerated, or blast phase Ph+ chronic myelogenous leukemia (CML) in patients with resistance or intolerance to prior therapy.

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS:

- An ONDQA chemistry filing review was performed and no microbiology issues were highlighted.
- The submission was provided in electronic eCTD format accessible through EDR.
- An information request was transmitted via the Division Project Manager to the applicant on 16 April 2012 requesting the removal of (b) (4) and inclusion of MLT within the long term stability program at a minimum of the T=0 time point. The applicant responded in the 16 May 2012 and 31 May submissions. Their responses are reviewed within the body of this report.

Filename: N203341N000R1.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 – (b) (4)

[redacted]

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
N/A

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/s/

ROBERT J MELLO
06/12/2012

JOHN W METCALFE
06/12/2012
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 203-341 **Applicant: Wyeth Pharmaceuticals, Inc.** **Letter Date:** 17 November 2011

Drug Name: BOSULIF® **NDA Type: 505(b)(1)** **Stamp Date:** 17 November 2011

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		Section 3.2.P.2.5, and Section 3.2.P.8 pages 3-6
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		Section 3.2.P.3.3, pages 1-3.
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?		X	No information submitted
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?	-	-	Not Applicable
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?		X	No microbial control specifications were submitted.
7	Has the applicant submitted the results of analytical method verification studies?	-	X	No methods related to microbial control were submitted
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	-	-	Not Applicable
9	Is this NDA fileable? If not, then describe why.	X		**The Application is fileable** but additional information will be required for a complete review of the submission.

Additional Comments: see below.

Robert J. Mello, Ph.D. Senior Review Microbiologist Date

Stephen Langille, Ph.D. Senior Review Microbiologist Date

Product Quality Microbiology Assessment

The drug product is an immediate release film coated tablet containing either 100mg or 500mg of bosutinib. (b) (4) There was no information on the environmental controls (air/surface/water) within the manufacturing environment. There were no specifications for microbial limits of the drug product, nor was there any justification for not having such a microbial limit specification. The following information should be requested from the Applicant:

> **Please provide a release specification for microbial limits of the drug product or provide an acceptable justification, which would include appropriate supportive data, for not having such a microbial limit specification.**

[END]

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/s/

ROBERT J MELLO
12/20/2011

STEPHEN E LANGILLE
12/20/2011