CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204114Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

30 November 2012

NDA: 204114/N-000

Drug Product Name
Proprietary: N/A.
Non-proprietary: Trametinib.

Review Number: 1.

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
02 AUG 2012	03 AUG 2012	06 AUG 2012	09 AUG 2012
28 SEP 2012	28 SEP 2012	N/A	N/A

Applicant/Sponsor
Name: GlaxoSmithKline, LLC.
Address: One Franklin Plaza,
200 North 16th St.
Philadelphia, PA 19102
Representative: Dori Roberts
Telephone: 919-483-6612

Name of Reviewer: John W. Metcalfe, Ph.D.

Conclusion: Recommend approval.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: 505(b)(1) NDA.

2. SUBMISSION PROVIDES FOR: Marketing authorization.

3. MANUFACTURING SITE:
GlaxoSmithKline Manufacturing SpA
Strada Provinciale Asolana, 90
San Polo di Torrile
Parma, 43056 Italy

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:
- Tablet.
- Oral administration.
- 0.5, 1 and 2 mg.

5. METHOD(S) OF STERILIZATION: The drug product is not sterile.

6. PHARMACOLOGICAL CATEGORY: Anti-cancer product.

B. SUPPORTING/RELATED DOCUMENTS: None.

C. REMARKS: The NDA is submitted electronically in the CTD format.

A Microbiology Information Request was forwarded to the applicant by the ONDQA Project Manager on 17 September 2012. Following is the IR:

A microbiology review of NDA 204114 is in progress. Following is a comment and request for additional information:

Your proposal to forgo performance of microbial limits testing on the finished drug product is acceptable based on the drug substance and drug product manufacturing processes, and the dry nature of the drug product. However, we suggest that microbial limits testing should be performed at the initial time point (at a minimum) on stability samples as a periodic measure of the microbiological quality of the drug product.

- *Provide a commitment to amend the drug product stability testing protocol with test methods and acceptance criteria for microbial limits testing.*

The applicant amended the NDA with a response to this request on 28 September 2012. The responses are summarized and reviewed in appropriate sections of this review.

File Name: N204114R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability – NDA 204114/N-000 is recommended for approval on the basis of issues pertaining to 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 is manufactured using current technology for drug tablets. Reference is made to Section P.3.3 for a detailed description of this process.

B. Brief Description of Microbiology Deficiencies – There are no microbiology deficiencies identified.

C. Assessment of Risk Due to Microbiology Deficiencies – Not applicable.

III. Administrative

A. Reviewer's Signature _____

John W. Metcalfe, Ph.D.
Senior Microbiology Reviewer
CDER/OPS/NDMS

B. Endorsement Block_____

Stephen E. Langille, Ph.D.
Senior Microbiology Reviewer
CDER/OPS/NDMS

C. CC Block

N/A

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/s/

JOHN W METCALFE
11/30/2012

STEPHEN E LANGILLE
11/30/2012

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 204114. **Applicant:** GlaxoSmithKline LLC. **Letter Date:** 02 August 2012.

Drug Name: Trametinib. **NDA Type:** Priority. **Stamp Date:** 03 August 2012.

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	See summary comment below.
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		Module 3.2.P.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	See summary comment below.
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	Not applicable to product dosage form.
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?		X	See summary comment below.
7	Has the applicant submitted the results of analytical method verification studies?		X	See summary comment below.
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?			This reviewer is not aware of any pre-submission meetings and/or discussions.
9	If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data?		X	Not applicable to product dosage form.
10	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: The drug product is a tablet. The lack of microbiology information in the NDA identified above does NOT preclude the filing of the NDA since the product is a non-sterile drug. The reviewer will decide during the review cycle whether the applicant's proposal to not perform microbial limits release testing is acceptable.

27 August 2012.

John W. Metcalfe, Ph.D. Date
Senior Microbiology Reviewer, CDER/OPS/NDMS.

27 August 2012.

Stephen E. Langille, Ph.D. Date
Senior Microbiology Reviewer, CDER/OPS/NDMS.

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/s/

JOHN W METCALFE
08/27/2012

STEPHEN E LANGILLE
08/29/2012