CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

200678Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

28 SEP 2010

NDA: 200-678

Drug Product Name
Proprietary: [redacted] (b) (4) (proposed)
Non-proprietary: Saxagliptin/metformin HCl extended-release

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
29 DEC 2009	29 DEC 2009	2 FEB 2010	17 FEB 2010
23 APR 2010	23 APR 2010	N/A	N/A
24 SEP 2010	24 SEP 2010	N/A	N/A

Applicant/Sponsor
Name: Bristol-Myers Squibb Co.
Address: P.O. Box 4000
Princeton, NJ 08543-4000
Representative: Pamela J. Smith, M.D.
Telephone: 609-252-5228

Name of Reviewer: Jessica G. Cole

Conclusion: Recommend approval.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original NDA

2. SUBMISSION PROVIDES FOR: New fixed-dose combination product.

3. MANUFACTURING SITE: Bristol-Myers Squibb
4601 Highway 62 East
Mount Vernon, IN 47620 USA

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

- Oral tablet
- 5/500 mg, 5/1000 mg, 2.5/1000 mg saxagliptin/metformin HCL-XR

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

6. PHARMACOLOGICAL CATEGORY: Indicated for Type 2 diabetes treatment.

B. SUPPORTING/RELATED DOCUMENTS: None.

C. REMARKS:

The following microbiology information request was included in the 74-day letter to the applicant.

Reviewer Comment

Please provide the following information:

1. The [redacted] (b) (4) in the finished drug product.
2. The microbial limits test validation studies or a summary of these studies.
3. The microbial limits testing protocols 5450A, 249965, 249966, and 249967.
4. A justification for only performing microbial limits testing [redacted] (b) (4) during routine production.

A response was received 23 April 2010 and the information was incorporated into the relevant sections of this review.

A second comment was sent to the sponsor through the project manager on 7/7/10:

Reviewer Comment

[redacted] (b) (4)

[redacted] (b) (4)

. The product specification should state that the product will meet the requirements of USP<1111>, if tested. These process controls, tests and acceptance criteria should be identified in the batch release criteria, and include, for example:

- Microbial limits data for critical raw materials,

- Microbiological environmental monitoring data for critical processing steps that can be related to the batch, and
- In-process control parameters (b) (4)) that may affect product quality microbiology.

In addition, microbial limits testing should be performed at the initial time point (at a minimum) on stability samples.

A response was received on 24 September and the response was incorporated into the relevant sections of this review.

filename: N200678R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability – Recommended for approval on the basis 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 is a (b) (4) tablet manufactured (b) (4)

B. Brief Description of Microbiology Deficiencies – Not applicable.

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

III. Administrative

A. Reviewer's Signature _____
Jessica G. Cole, Ph.D.

B. Endorsement Block _____
Stephen Langille, Ph.D.
Senior Microbiology Reviewer

C. CC Block
N/A

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