CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204026Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

September 6, 2012

NDA: 204026

Drug Product Name
Proprietary: Not available
Non-proprietary: Pomalidomide

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
4/10/2012	4/10/2012	6/06/2012	6/08/2012
8/24/2012	8/24/2012	N/A	N/A
8/30/2012	8/30/2012	N/A	N/A

Submission History (for amendments only)
None

Applicant/Sponsor
Name: Celgene Corporation
Address: 86 Morris Avenue, Summit, N.J. 07901
Representative: Paul McInulty, Director, Regulatory Affairs.
Telephone: 908 219 0743

Name of Reviewer: Steven P. Donald, M.S.

Conclusion: Recommended for approval.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original NDA

2. SUBMISSION PROVIDES FOR: The manufacture of an oral drug

3. MANUFACTURING SITE:
Celgene International Sarl, Route de Perreux 1, Boudry 2017, Switzerland, and (b) (4)

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Gelatin capsule filled with (b) (4) oral, 1 mg, 2 mg, 3 mg and 4 mg dose

5. METHOD(S) OF STERILIZATION: Non sterile

6. PHARMACOLOGICAL CATEGORY: Immunomodulator

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: NDA 204026 was submitted electronically in CTD format. A information request for information on microbial limits testing was sent to the applicant on 7/13/2012 and a response was received on 8/10/2012 by email, and the official submission was received on August 24, 2012. A subsequent information request was provided to the sponsor on August 27, 2012 and a response was received on 8/30/2012. The provided information will be included after each comment in the body of the review.

filename: N204026r1.doc

Reference ID: 3185191

Executive Summary

I. Recommendations

A. Recommendation on Approvability –
NDA 204026 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 drug product is a capsule for oral administration. The capsule contents are (b) (4) before filling.

B. Brief Description of Microbiology Deficiencies -
No deficiencies were identified based upon the information provided.

C. Assessment of Risk Due to Microbiology Deficiencies –
N/A

III. Administrative

A. Reviewer's Signature _____
Steven P. Donald, M.S.

B. Endorsement Block_____
Bryan Riley, Ph.D.
Team Leader

C. CC Block
N/A

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/s/

STEVEN P DONALD
09/06/2012

BRYAN S RILEY
09/06/2012
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 204026 **Applicant: Celgene Corp.** **Letter Date:** 4/10/2012

Drug Name: Pomalidomide (capsules) **NDA Type: 505 (b)(1)** **Stamp Date:** 4/10/2012

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		Information is organized but microbiology information is limiting
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		The manufacturing process is described but microbiological controls are not; Section 3.2.P.3.3, manuf-process-and-controls.pdf;
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?		X	"The manufacturing process will be validated prior to launch"; 3.2.P.3.5 of both manufacturing sites.
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?			N/A
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?		X	(b) (4) and Celgene sites: No microbiological specifications for drug product. The applicant proposes not to perform routine microbiological testing of the drug product; in process

	Content Parameter	Yes	No	Comments
				testing is reported but not described; excipient microbiological limits or testing is not described.
7	Has the applicant submitted the results of analytical method verification studies?		X	(b) (4) and Celgene sites: No microbiological methods verification information provided.
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?			N/A
9	If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data?			N/A
10	Is this NDA fileable? If not, then describe why.	X		

Additional Comments:
The drug product is manufactured at two different locations: (b) (4) and Celgene International, Sarl, Switzerland.

Under Justification of specifications (justification-of-specifications.pdf, pg. 4/4, both drug product manufacturing sites), the applicant states that microbial limits testing has been conducted throughout development as well as during process validation; it is also stated that all lots tested to date have met USP <61> and USP <62> requirements. It is proposed not to include microbial limits in the specifications of Pomalidomide drug product.

Batch analysis for the 1 mg, 2 mg, 3 mg and 4 mg configurations manufactured at the (b) (4) site lists Microbial Limits testing and results as conforming to USP <61> and USP <62>; not all batches of each configuration list both tests (early batches of each configuration list only USP <61>); early batches of the 1 mg configuration list neither test. Batch analysis of batches manufactured at the Celgene site do not list any microbiological testing or results.

In Section 3.2.P.2, Pharmaceutical Development (micro-attrib.pdf, pg. 1/1; both manufacturing sites) the applicant state that during development, the drug substance and drug product were monitored for microbial limits according to USP <61> and USP <62>. The compendia excipients are controlled according to the current NF monographs, including microbial limits testing, although testing details or limits are not provided. The microbial attributes of the capsule shells are controlled as described in Section 3.2.P.4.4 and reference USP/Ph.Eur. for tests and acceptance criteria. It is proposed that routine microbiological testing not be performed as the data generated to date demonstrate that batches consistently meet the microbial limits requirements.

The manufacture of the oral drug product appears to be well controlled. The NDA is fileable without the specification of microbial limits. The reviewer will request the microbial limits information during the review of the NDA.

Reviewing Microbiologist: Steven P. Donald, M.S. Date

Microbiology Team Leader: Bryan Riley, Ph.D. Date

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/s/

STEVEN P DONALD
06/22/2012

BRYAN S RILEY
06/22/2012
I concur.