CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

206256Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

Product Quality Microbiology Review

08 MAY 2014

NDA: 206256

Drug Product Name
Proprietary: Beleodaq™
Non-proprietary: Belinostat for Injection

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
08 Dec 2013	09 Dec 2013	09 Dec 2013	16 Dec 2013
28 Mar 2014	28 Mar 2014	N/A	N/A
25 Apr 2014	25 Apr 2014	N/A	N/A

Applicant/Sponsor
Name: Spectrum Pharmaceuticals, Inc.
Address: 157 Technology Drive
Irvine, CA 92618
Representative: Anil K. Hiteshi
Telephone: 949-743-9228

Name of Reviewer: Neal J. Sweeney, Ph.D.

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

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

2. SUBMISSION PROVIDES FOR: New drug product

3. MANUFACTURING SITE: (b) (4)

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Single use, 500 mg, lyophilized belinostat in 30 mL glass vial for intravenous infusion.

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

6. PHARMACOLOGICAL CATEGORY: Pan-histone deacetylase (HDAC) inhibitor, indicated for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma.

B. SUPPORTING/RELATED DOCUMENTS:
DMF (b) (4)

C. REMARKS:

(b) (4) Letter of Authorization (dated February 7, 2013) on behalf of Spectrum Pharmaceuticals, provided in Module 1.4.1., authorizes FDA to refer to DMF (b) (4) for (b) (4) information for the (b) (4) used for Belinostat for Injection.

A Microbiology Information Request was issued to the applicant on March 4, 2014, and the applicant forwarded responses on March 28, 2014 and April 25, 2014.

File name: N206256R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability - Recommended for 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) .

B. Brief Description of Microbiology Deficiencies – Based upon the information provided, no microbiology deficiencies were identified.

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

D. Contains Potential Precedent Decision(s)- ☐ **Yes** ☒ **No**
(If yes, provide a brief description and a reference to the page where the precedent is discussed in depth)

III. Administrative

A. Reviewer's Signature _____
Neal J. Sweeney, Ph.D.

B. Endorsement Block _____
John W. Metcalfe, Ph.D.

C. CC Block
N/A

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/s/

NEAL J SWEENEY
05/12/2014

JOHN W METCALFE
05/12/2014
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 206256 **Applicant:** Spectrum Pharmaceuticals Inc. **Letter Date:** 12/8/13

Drug Name: Belinostat for Inj (500 mg/vial) **NDA Type: 505(b)(2)** Standard **Stamp Date:** 12/9/13

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		eCTD
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		(b) (4)
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		
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		3.2.P.2. C/C integrity AET: N/A
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		3.2.P.5.1. (release and stability) sterility and endotoxin, 3.2.P.5.6 justification for sterility and endotoxin limit
7	Has the applicant submitted the results of analytical method verification studies?	X		3.2.P.5.3 (bioburden, sterility and endotoxin testing)
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	X		Micro reconstitution/dilution/storage study was requested during Dec. 10, 2009 CMC EOP2 Meeting. Micro study provided in Section 3.2.P.8.1 (See Additional Comments section below)
9	If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data?	X		Reconstitution with 9 mL sterile WFI and then stored up to (b) (4) at CRT. Further diluted in 250 mL saline LVP and stored up to (b) (4) (including 30 min infusion) at CRT. Micro study provided in Section 3.2.P.8.1 (See Additional Comments section below)

	Content Parameter	Yes	No	Comments
10	Is this NDA fileable? If not, then describe why.	X		

Additional Comments:

The December 10, 2009 End of Phase 2 CMC teleconference meeting minutes indicated that the Agency requested microbiological data supporting the proposed (b) (4) /RT storage of the reconstituted drug product. However, the current proposed product labeling specifies reconstitution with 9mL WFI and storage up to (b) (4) at RT, followed by further dilution in 250 mL Sodium Chloride Injection and subsequent storage of up to (b) (4) at RT prior to patient administration. The NDA submission contains study reports supporting the (b) (4) /RT storage of the reconstituted drug product and (b) (4) /RT storage of the admixed solution. USP <51> Antimicrobial Effectiveness Testing was performed for both storage studies.

23 January 2014

Neal J. Sweeney, Ph.D., Reviewing Microbiologist — Date

Bryan S. Riley, Ph.D., Acting Team Leader — Date

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

NEAL J SWEENEY
01/24/2014

BRYAN S RILEY
01/24/2014
I concur.