CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

205582Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

Product Quality Microbiology Review

13 NOV 2013

NDA: 205582

Drug Product Name
Proprietary: (none)
Non-proprietary: Decitabine for Injection

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
27 March 2013	27 March 2013	15 April 2013	18 April 2013
02 Nov 2013	04 Nov 2013	05 Nov 2013	05 Nov 2013

Applicant/Sponsor
Name: Sun Pharma Global FZE
Address: Office #43, Block Y, SAIF Zone, P. O. Box # 122304, Sharjah, U.A.E.
Representative: Karin A. Kook, PhD
Salamandra, LLC
One Bethesda Center, 4800 Hampden Lane, Suite 900
Bethesda, MD 20814-2998
Telephone: 301-652-6739

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

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: 505 (b) (2) Original NDA

2. SUBMISSION PROVIDES FOR: New drug product

3. MANUFACTURING SITE: Sun Pharmaceutical Industries Ltd.
Halol-Baroda Highway
Halol-389 350, Gujarat, India 389350

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: single-dose, 50 mg, lyophilized decitabine in 20 mL glass vial for intravenous infusion, packaged with 10 mL diluent vial (68 mg monobasic potassium phosphate and 11.6 mg sodium hydroxide)

5. METHOD(S) OF STERILIZATION:
Decitabine for Injection, 50 mg/vial: sterile filtration, lyophilization, and (b) (4) processing
Diluent for Decitabine for Injection, 50 mg/vial: (b) (4) sterilization

6. PHARMACOLOGICAL CATEGORY: Antineoplastic/cytotoxic nucleoside metabolic inhibitor, indicated for treatment of myelodysplastic syndromes (MDS).

B. SUPPORTING/RELATED DOCUMENTS:
NDA 21-790 DACOGEN® (decitabine) for Injection (RLD)
DMF (b) (4)

C. REMARKS: The proposed indications and dosing instructions for Sun's Decitabine for Injection are identical to those of the currently approved DACOGEN® product. Both products are lyophilized powders containing 50 mg of decitabine in a 20 mL glass vial. However, unlike Sun's new drug product, Dacogen® contains monobasic potassium phosphate and sodium hydroxide (b) (4) (b) (4) in the vial containing the drug product. In Sun's product, the diluent contains monobasic potassium phosphate and sodium hydroxide. Upon reconstitution with 10 mL Water for Injection, USP (in the case of Dacogen®) or a diluent (in the case of Decitabine for Injection), both result in a solution of identical composition.

Letters of Authorization (dated January 14, 2013), provided in Module 1.4.1.1, authorized FDA to refer to DMF (b) (4) for Decitabine for Injection and Diluent for Decitabine for Injection.

A Microbiology Information Request was issued to the applicant on Oct 10, 2013, and the applicant forwarded responses on Nov. 2, 2013.

filename: N205582R1.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 – The drug product is (b) (4) (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 _____
Bryan S. Riley, Acting Team Leader

C. CC Block
N/A

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/s/

NEAL J SWEENEY
11/14/2013

BRYAN S RILEY
11/14/2013
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 205583 **Applicant:** Sun Pharma Global **Letter Date:** 3/25/13

Drug Name: Decitabine for Inj **NDA Type:** 505(b)(2) Standard **Stamp Date:**3/27/13

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 format
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		DP: filtration (b) (4) processing Diluent (b) (4) sterilization
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		3.2.P.3.5. for both DP and Diluent steril (b) (4) processes
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		C/C integrity for both DP and Diluent in both Sections 3.2.P.3.5 and 3.2.P.2. Single dose, no preservative
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 3.2.P.8.1 (Stability) for both DP and Diluent. Justification of endotoxin specs (DP and Diluent) in 3.2.P.5.6
7	Has the applicant submitted the results of analytical method verification studies?	X		3.2.P.5.3 sterility and endotoxins test verification studies for both DP and Diluent
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	N/A	N/A	No requested Micro studies were indicated in the Pre-NDA meeting minutes.
9	If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data?	X		Admix challenge studies in 3.2.P.2. Max storage 7 hrs at 2ºC-8ºC
10	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: (none)

Neal J. Sweeney, Ph.D., Reviewing Microbiologist Date 4/30/2013

Bryan S. Riley, Ph.D., Reviewer/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
05/01/2013

BRYAN S RILEY
05/01/2013
I concur.