CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

207026Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

Product Quality Microbiology Review

30 October 2014

NDA: 207-026/N000

Drug Product Name
Proprietary: Phoxillum BK4/2.5
Phoxillum B22K4/0
Non-proprietary: NA

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
13 March 2014	13 March 2014	13 March 2014	13 March 2014
28 August 2014	28 August 2014	NA	NA
05 September 2014	05 September 2014	NA	NA

Submission History (for 2nd Reviews or higher) – NA

Applicant/Sponsor
Name: Gambro Lundia AB
Address: PO Box 10 101
Lund, Sweden SE-22 10
US Agent: Fei Law, Quality and Regulatory Manager
US Solutions
1845 Mason Avenue
Daytona Beach, FL 32117
Telephone: (386) 481-1143

Name of Reviewer: Denise A. Miller

Conclusion: Recommended for approval from a quality microbiology perspective.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original new drug application

2. SUBMISSION PROVIDES FOR: The application provides for the manufacture and marketing of the subject drug product.

3. MANUFACTURING SITE:
Gambro Renal Products, Inc.
1845 Mason Avenue
Daytona Beach, Fl. 32117
FEI # 1051129

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

- Dosage Form: Sterile solution in a 5L two compartment bag
- Route of Administration: Extracorporeal circuit
- Strength/Potency: BK4/2.5 and B22K4/0

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

6. PHARMACOLOGICAL CATEGORY: replacement solution in Continuous Renal Replacement Therapy (CRRT) (b) (4)

B. SUPPORTING/RELATED DOCUMENTS:
PrismaSol (NDA 21-703)
PrismaSATE (510K K013448)

C. REMARKS:
This product is a slight modification to the formulation from the currently marketed products by this sponsor.
Two information requests (IR) were sent:
IR dated 08 August 2014 with a response on 28 August 2014
IR dated 25 August 2014 with a response on 05 September 2014
The IRs and responses are reviewed in the appropriate sections of this review.

filename: N207026N000R1.docx

Reference ID: 3656857

Executive Summary

I. Recommendations

A. Recommendation on Approvability - Recommended for approval from a quality microbiology perspective.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable - NA

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – This product is (b) (4)

B. Brief Description of Microbiology Deficiencies – There were no deficiencies identified in the information submitted.

C. Contains Potential Precedent Decision(s)- ☐ **Yes** ☒ **No**

III. Product Quality Microbiology Risk Assessment

A. Initial Product Quality Microbiology Risk Assessment

CQA	Risk Factor	Prob. of Occ. (O)	Modifier for O[3, 4, 5]	Severity of Effect (S)	Detect. (D)	Risk Priority Number[6] (RPN)	Additional Review Emphasis based on Risk (in addition to normal review process)
(b) (4)							

Reference ID: 3656857

B. Final Risk Assessment – The product risk was minimized though the validation of the [redacted] (b) (4) A separate Container Closure Integrity (CCI) study was not included in this application as the CCI was previously established and reviewed for this product family in a referenced NDA. The shelf life CCI was established in the stability program. The risk of endotoxin contamination is controlled through testing and the manufacturing process for the container closure does not lend itself to endotoxin contamination of the final drug product.

IV. Administrative

A. Reviewer's Signature _____

Denise A. Miller
Microbiologist, OPS/NDMS

B. Endorsement Block_____

Neal J. Sweeney
Senior Microbiologist, OPS/NDMS

C. CC Block

N/A

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/s/

DENISE A MILLER
11/12/2014

NEAL J SWEENEY
11/12/2014
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number:207-026 **Applicant:** Gambro Lundia AB **Letter Date:** 13 March 2014

Drug Name: **NDA Type:**505 (b)(2) **Stamp Date:** 13 March 2014

Phoxilium BK 4/2.5

Phoxilum B2K4/0

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?	√		e-CTD format
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	√		
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	√		(b) (4) yes (report DP573-1-PQ-FR
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?		√	
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity (CCI) studies?		√	PE: NA CCI: see comment #3 below
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	√		
7	Has the applicant submitted the results of analytical method verification studies?		√	Method suitability studies for endotoxin and sterility test was not located in the submission. See comment #4 below
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	NA		
9	If sterile, are extended post-constitution and/or post-dilution hold time in the draft labeling supported by microbiological data?		√	See comment #2 below.
10	Is this NDA fileable? If not, then describe why.	√		

Additional Comments:
1) This product is for fluid replacement during continuous renal replacement therapy (CRRT) in the extracorpeal blood flow circuit. Similar products are currently being manufactured by The sponsor Gambro (NDA 21-703 PrismaSol Solutions) which is referenced in this submission. The proposed new product, Phoxilium [redacted] (b) (4) phosphate added at 1 mmol/L.

2) The Container Closure system is a two compartment bag [redacted] (b) (4) Mixing of the two components is in a closed system; therefore post-constitution hold times are not applicable to this product.

3) As the proposed container closure system is currently used for an approved product and is similar to the proposed product, CCI testing is not required for this application. The integrity of the container closure through the shelf life will be demonstrated in the stability program

4) The method suitability for endotoxin and sterility testing will be requested.

Denise A. Miller
Microbiologist, OPS/NDMS

Bryan S. Riley, Ph.D.
Senior Microbiologist, OPS/NDMS

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/s/

DENISE A MILLER
04/24/2014

BRYAN S RILEY
04/24/2014
I concur.