



**DBSQ/OCBQ ANALYTICAL METHOD REVIEW MEMO**

**To:** The file STN 125757

**From:**

Reviewer	Role	Date Finalized	Stamp	Supervisor	Stamp
Kouassi Ayikoe, Ph.D.	Lead Reviewer	03/17/2023		Kenneth S. Phillips, Ph.D.	
Brianna R. Davis	Reviewer	03/22/2023		James L. Kenney, D.Sc.	

**Through:** Maryna Eichelberger, Ph.D., Division Director, CBER/OCBQ/DBSQ

**Product:** VOWST, SER-109 (Purified Microbiome Therapeutic, (b) (4) )

**Applicant:** Seres Therapeutics Inc.

**Subject:** Review of analytical methods used for SER-109 Purified Microbiome Therapeutic, Oral (VOWST™) drug substance and drug product lot release.

**Recommendation:** Approval

**Executive Summary:**

On August 26, 2022, Seres Therapeutics submitted an original Biologics License Application (BLA STN 125757) for SER-109 (Purified Microbiome Therapeutic, (b) (4) ) for recurrent *Clostridioides difficile* infection (rCDI).

The following analytical methods used for lot release of SER-109 (Purified Microbiome Therapeutic, (b) (4) ) were reviewed:

1. Test for Specified Microorganisms (DP), (Brianna R. Davis)
2. Identity ((b) (4) DP), (Kouassi Ayikoe)
3. (b) (4) , (Kouassi Ayikoe)
4. (b) (4) , (Kouassi Ayikoe)
5. Residual Solvent (DP), (Kouassi Ayikoe)
6. (b) (4) (DP), (Kouassi Ayikoe)
7. Appearance & Physical Characteristics (DP); (Kouassi Ayikoe)
8. (b) (4) (DP); (Kouassi Ayikoe)

**Conclusion:** The analytical methods and their validations and/or qualifications reviewed for the SER-109 drug substance and drug product were found to be adequate for their intended use.

### Documents Reviewed

Information in sections of the original submission that describe control of DS and DP (3.2.S.4 and 3.2.P.5, respectively), including descriptions of DS and DP specifications, analytical procedures of DS and DP and validation of these analytical procedures were reviewed. Additional information in amendments specified by each reviewer were also reviewed.

### Background

Seres Therapeutics has developed VOWST, a purified microbiome therapeutic, indicated to prevent *Clostridioides difficile* infection (CDI) in adults with recurrent CDI. VOWST (SER-109) drug product (DP) contains purified Firmicutes bacterial spores purified from the stool of qualified human donors, formulated in glycerol in saline and encapsulated for oral administration. The SER-109 DP contains  $1 \times 10^6$  to  $3 \times 10^7$  spore colony forming units (SCFU) per capsule as the active ingredient. The SER-109 drug substance is formulated in a (b) (4) (formulated bulk) filled into white inner capsule and sealed. Non active ingredients are non-aqueous glycerol ( (b) (4) ), sodium chloride (b) (4) , inner capsule to hold the spores in suspension, (b) (4) as (b) (4) , outer capsule for appearance and blue imprint of SER-109.

This review covers the analytical method validations or qualifications for lot release testing of SER-109 DS, SER-109 DP, and excipients.

### Review Narrative

#### 1. Test for Specified Microorganisms (DP)

The test for specified microorganisms is performed on the DP at Seres facilities in Cambridge (b) (4) , Massachusetts. Specifications of (b) (4) must be met for lot release of VOWST™.

#### Method

The test for specified microorganisms performed in accordance with (b) (4) ensures the method can detect the presence of specified microorganisms that are known to be (b) (4)

(b) (4). The method is described in more detail below together with the tests that were performed to determine suitability of the test method for its intended use.

Test for Specified Microorganisms Qualification

Cambridge, MA facility qualified their test for specified microorganisms using VOWST™ DP by (b) (4)

[Redacted]

[Redacted]

[Redacted]

(b) (4)

Conclusion

The method suitability tests were performed and found compliant with (b) (4) . The test results indicate there is no product inhibition of microorganism growth, thus indicating the tests for specified microorganism is appropriate under the actual conditions of use at the Cambridge (b) (4) , MA facilities.

**2. Identity ((b) (4) DP)**

The identity (ID) of SER-109 (b) (4) drug product (DP) is determined by (b) (4) . The specification of the ID test is “ (b) (4) ”.

Method

A detailed description of method (b) (4) assay ((b) (4) ) for (b) (4) DP was provided. Samples are (b) (4)

(b) (4)

Method Validation

The analytical method was validated at Seres Therapeutics Inc., Cambridge Massachusetts. A validation protocol PROT-0104 was established and executed for the (b) (4) assay ((b) (4) ) with (b) (4) drug

product (DP) samples. The results are documented in the report RPT-00036. The validation study aligned with (b) (4) guidelines. (b) (4) DP samples were tested in studies of assay specificity, linearity, accuracy, precision (repeatability and intermediate precision), robustness, limit of detection (LOD), limit of quantitation (LOQ) and range. The following samples from different manufacturing stages were used for the validation: (b) (4)

Specificity of the method was demonstrated by (b) (4)

The specificity of the method was demonstrated.

Linearity was demonstrated from (b) (4)

Accuracy was demonstrated by (b) (4)

The acceptance criteria of (b) (4) are met for (b) (4) DP.

Precision: Repeatability of the method was evaluated from the (b) (4)

Intermediate precision of the (b) (4) DP assay was demonstrated by (b) (4)

[Redacted]

Range of the assay is based on (b) (4)

[Redacted]

Limit of detection (LOD) was calculated as (b) (4)

[Redacted]

Limit of quantitation (LOQ) was determined (b) (4)

[Redacted]

Robustness of the method was evaluated by (b) (4)

[Redacted]

the assay at (b) (4) was demonstrated.

Robustness of

Method Transfer

(b) (4)

(b) (4)

[Redacted]

[Redacted]

Conclusion:

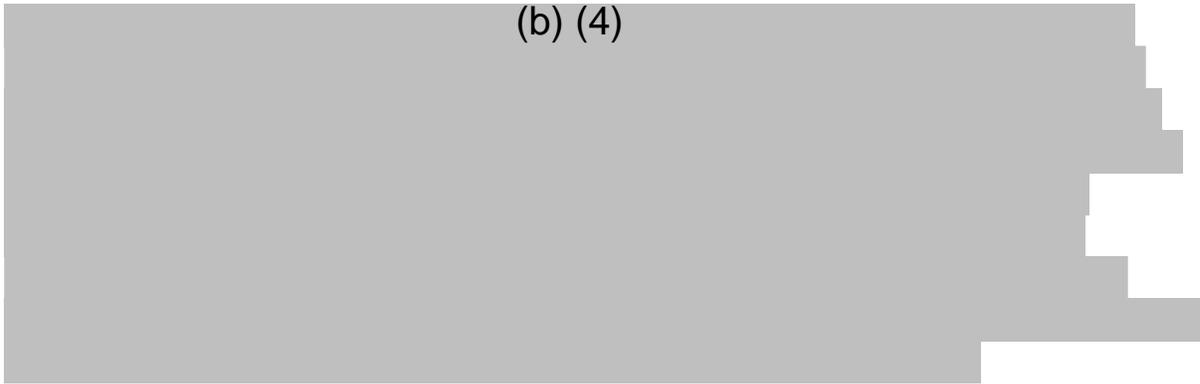
The (b) (4) method for determination of spores in Seres Therapeutics (b) (4) drug product is adequately described. The validation data demonstrate that it is suitable for identity testing of (b) (4) DP.

(b) (4)

[Redacted]

5 pages have been determined to be not releaseable: (b)(4)

(b) (4)



**7. Appearance and Physical characteristics (DP)**

The specification for Appearance and physical characteristics of SER-109 DP is: White, opaque capsules consistent with size 00 standard; possible (b) (4); and printed with “SER-109” in blue ink on capsule body.

Method

The appearance assay TM-0009 for SER-109 capsules is a visual examination for conformance to intended product image. No formal assay validation was performed; the DP is examined for defects on capsules imprinted with SER-109. (b) (4)



Method Validation

No validation nor evaluation was performed on the TM-0009. Data from batch records with lot # (b) (4) verified that the test is suitable for determining appearance of DP.

Conclusion:

With all the study parameters passed the acceptance criteria, and the (b) (4) sample type as per TM-0009, this visual appearance test is suitable for evaluating the final DP. (b) (4) must meet the acceptance criterion.

8. (b) (4) (DP)

(b) (4)

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(b) (4)

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