

## DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

**To:** The file STN 125772/0

**From:**

Reviewer	Role	Date finalized	Stamp	Supervisor	Stamp
Hsiaoling Wang	Lead Reviewer	10/17/2022		Tao Pan	
Simleen Kaur	Reviewer	09/20/2022		James Kenney	
Esmeralda Alvarado Facundo	Reviewer	11/01/2022		Muhammad Shahabuddin	

**Through** Maryna Eichelberger, Ph.D.  
Division Director, DBSQC/OCBQ

**Applicant:** CSL Behring

**Subject:** Review of Analytical Methods used for lot release of HEMGENIX (etranacogene dezaparvovec) (b) (4) Drug Product Lot Release

**Recommendation:** Approval

### Executive Summary:

The following analytical methods used for lot release of HEMGENIX and the associated analytic method validations or qualifications, were reviewed:

1. Bioburden (Simleen Kaur)
2. Sterility (Simleen Kaur)
3. Endotoxin (Simleen Kaur)
4. (b) (4) (Simleen Kaur)
5. Determination of (b) (4) in rAAV Samples (Hsiaoling Wang)
6. (b) (4) (Hsiaoling Wang)
7. Appearance including color and clarity and visible particulates (Hsiaoling Wang)
8. (b) (4) (Hsiaoling Wang)
9. (b) (4) (Hsiaoling Wang)
10. Determination of Sucrose Concentration by (b) (4) (Hsiaoling Wang)
11. Polysorbate-20 Concentration by (b) (4) (Hsiaoling Wang)

12. (b) (4) (Hsiaoling Wang)
13. Extractable Volume (Hsiaoling Wang)
14. (b) (4) (Esmeralda Alvarado Facundo)
15. (b) (4) (Esmeralda Alvarado Facundo)

**Conclusion:** The analytical methods and their validations and/or qualifications reviewed for the HEMGENIX (b) (4) drug product were found to be adequate for their intended use.

#### Documents Reviewed

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

#### Background:

CSL Behring (CSL) submitted a BLA STN 125772 for HEMGENIX (etranacogene dezaparvovec), an adeno-associated virus vector (AAV) based gene therapy, on March 22, 2022. This product is indicated for treatment of adults with Hemophilia B (congenital Factor IX deficiency) (b) (4)

who currently use Factor IX prophylaxis therapy, or have current or historical life-threatening hemorrhage, or repeated, serious spontaneous bleeding episodes

(b) (4)

The drug product (DP) is a preservative-free, liquid formulation with a nominal concentration of  $1 \times 10^{13}$  genome copies/mL of AAV5-hFIXco-Padua in a sterile (b) (4) solution containing 5% (w/v) sucrose and 0.02% (v/v) PS-20 in a single-use 10 mL glass vial stored at 2-8°C.


The facilities listed below perform tests for DS or/and DP lot release.

Location	Responsibility
uniQure, Inc. Lexington, MA	Drug substance and drug product release testing
(b) (4)	
(b) (4)	
(b) (4)	Drug product release testing: Sterility
(b) (4)	


## 1. Bioburden Method (Simleen Kaur)

Method

(b) (4)



(b) (4)



### Conclusion





The method suitability test was performed and compliant with (b) (4) and the test results indicate there is no product inhibition on microorganism growth, thus indicating the (b) (4)

(b) (4) sterility test method is appropriate under the actual conditions of use.

## 2. Sterility Method (Simleen Kaur)

Method

(b) (4)



### Conclusion


The method suitability test was performed and compliant with (b) (4) and the test results

indicate there is no product inhibition of microorganism growth, thus indicating the (b) (4) sterility test method is appropriate under the actual conditions of use.

### 3. Endotoxin (Simleen Kaur)

#### Method

(b) (4)




### Conclusion

The method suitability test was performed and compliant with (b) (4) and the test results indicate there is no product interference from (b) (4) DP test samples, thus indicating the (b) (4) test method is appropriate under the actual conditions of use.

#### 4. (b) (4) Method (Simleen Kaur)






Method

(b) (4)





(b) (4)



**7. Appearance including color and clarity (b) (4) DP) and visible particulates (DP)  
(Hsiaoling Wang)**

The specification of color for both (b) (4) DP is colorless liquid; the specification of clarity for (b) (4) DP is < reference suspension IV; and the specification of visible particles for DP is essentially free of visible particulates. The test is performed at uniQure, Inc., in Lexington, MA.

Method

Analytical procedure QC-SOP-0010 “Visual Appearance of (b) (4) Drug Product” was provided in amendment 13, which describes tests of color, clarity for (b) (4) DP and determination of visible particles for DP according to (b) (4) respectively.





purpose.

(b) (4)

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

#### 10. Determination of Sucrose Concentration by (b) (4) DP) (Hsiaoling Wang)

Sucrose is one of the matrix components for HEMGENIX, its concentration is determined according to (b) (4) DP samples in initial submission, and the SOP (QC-SOP-0011 Rev.3) was provided in amendment 15. The specification of sucrose for (b) (4) DP is (b) (4) . The test is performed at uniQure, Inc., in Lexington, MA.

Method

(b) (4)

[REDACTED]

[REDACTED]

(b) (4)

[REDACTED]

[REDACTED]

#### Conclusion

Based on the information provided in the original BLA and amendment, the method has been validated for its intended purpose.

#### **11. Polysorbate-20 Concentration by (b) (4) DP) (Hsiaoling Wang)**

Polysorbate-20 (PS-20) is added to the (b) (4) DP is

(b) (4) . The test is performed at uniQure, Inc., in Lexington, MA.

#### Method

A brief description of the method was presented in the initial submission, and the analytical procedure (QC-SOP-0044 Rev.3) was provided in amendment 13.

(b) (4)

[REDACTED]

1 page determined to be not releasable: (b)(4)

(b) (4)

(b) (4)

Conclusion

Based on the information provided in the original BLA and amendments, the method has been validated for its intended purpose.

12. (b) (4) (DP) (Hsiaoling Wang)

(b) (4)

(b) (4)

(b) (4)

### 13. Extractable Volume (DP) (Hsiaoling Wang)

The specification of extractable volume for DP is  $\geq 10.0$  mL. The test is performed at uniQure, Inc., in Lexington, MA.

#### Method

The extractable volume is determined according to (b) (4) for DP. The content of a DP vial (b) (4)

(b) (4)

#### Conclusion

Based on the information provided in the original BLA and amendment, the method has been verified for its intended purpose.

### 14. (b) (4) (Esmeralda Alvarado Facundo)

(b) (4)

