



DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To: The file STN 125781

From:

Reviewer	Role	Date finalized	Stamp	Laboratory/Lab Chief	Stamp
Tao Pan Ph.D.	Lead Reviewer	03/14/2023		Kenneth S. Phillips, Ph.D.	
Simleen Kaur, M.S.	Reviewer	02/23/2023		James L. Kenney, D.Sc.	

Through Maryna Eichelberger, Ph.D.
Division Director, DBSQC

Applicant: Sarepta Therapeutics (Sarepta)

Subject: Review of Analytical Methods used for delandistrogene moxeparvovec (SRP-9001) Drug Substance (DS) and Drug Product (DP) Lot Release

Recommendation: Approval

Summary:

The following analytical methods used for lot release of delandistrogene moxeparvovec (SRP-9001) drug substance (DS) and drug product (DP) from Sarepta Therapeutics, Inc. (Sarepta), and the associated validations and qualifications, were reviewed:

1. (b) (4) (Tao Pan),
2. (b) (4) (Tao Pan),
3. (b) (4) (Tao Pan),
4. Appearance of DP (Tao Pan),
5. (b) (4) of DP (Tao Pan),
6. (b) (4) of DP (Tao Pan),
7. Particulate matter of DP (Tao Pan),
8. Extractable volume of DP (Tao Pan).
9. (b) (4) (Simleen Kaur)
10. (b) (4) (Simleen Kaur)
11. Endotoxin test of (b) (4) DP (Simleen Kaur)
12. Sterility of DP (Simleen Kaur)

Conclusion: The analytical methods and their validations and/or qualifications reviewed for delandistrogene moxeparvovec (SRP-9001) 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, 3.2.P.5, and 3.2.R respectively), including descriptions of DS and DP specifications, analytical procedures of DS and DP and validations of these analytical procedures were reviewed. Additional information in amendments specified by each reviewer were also reviewed.


Background:

SRP-9001 (delandistrogene moxeparvovec) is an adeno-associated virus (AAV) vector-based gene therapy intended to treat the Duchenne muscular dystrophy (DMD) by replacing dysfunctional or missing dystrophin protein with a functional shortened dystrophin, called SRP-9001-dystrophin, in cardiac, respiratory, and skeletal muscle. The (b) (4) of non-replicating, recombinant AAV vector particles containing the SRP-9001-dystrophin expression cassette construct; the DS is (b) (4), filtered and filled in vials as sterile DP for intravenous administration.




DBSQC reviews analytical methods used for release of DS and DP to ensure they are suitable for their intended use. Therefore, this review focuses on the qualification or validation of each method under actual conditions of use.

Review Narrative:

1. (b) (4)



(b) (4)



4. Appearance of DP


The appearance of the DP, including the color of vial cap, is determined by visual inspection, the release specification is “Clear, colorless liquid, may have some opalescence, may contain white to off-white particles” and “Cap color: Blue”.

Method:


Visual inspection for the appearance of DP is performed at (b) (4)



to examine attributes such as clarity, color, cap color, and visible particles of the DP final container. In (b) (4)




, the cap color of the final container is first confirmed to be BLUE; for visible particulates and foreign matter, samples are evaluated (b) (4)



Method Verification:

The analytical methods for DP appearance were verified for lot release testing at (b) (4), the verification reports were submitted in Amendment 15 as responses to the information request from FDA dated January 10. For the verification at (b) (4)




Conclusion:

Based on information provided, the appearance methods have been verified for release testing of SRP-9001 DP.

5. (b) (4) of DP
(b) (4)



(b) (4)



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7. Particulate Matter of DP

The particulate matter of SRP-9001 DP is determined by a (b) (4)



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Method:

The particulate matter test is performed for SRP-9001 DP at (b) (4)




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(b) (4)



(b) (4)

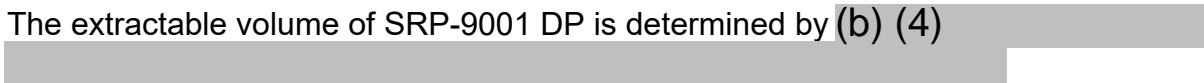


Conclusion:

Based on information provided, the particulate matter methods have been verified for the release testing of the SRP-9001 DP.

8. Extractable volume of DP

The extractable volume of SRP-9001 DP is determined by (b) (4)



Method:


The extractable volume test was performed for SRP-9001 DP at (b) (4)




Sufficient information has been provided for the methods.

Method Verification:

The extractable volume methods for DP were verified for lot release testing at (b) (4) the verification reports were submitted in Amendment 15 as a response to the information request from FDA dated January 10. For the verification at (b) (4)




(b) (4)

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Conclusion:

Based on information provided, the extractable volume methods have been verified for release testing of SRP-9001 DP.

(b) (4) (b) (4)

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(b) (4)



11. Endotoxin Method of (b) (4) DP


Endotoxin testing for SRP-9001 (b) (4)

DP testing is performed at (b) (4)




Method:

(b) (4)



1 page determined to be not releasable: (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 interference from (b) (4) DP test samples, thus indicating the (b) (4) BET test method is appropriate under the actual conditions of use.

12. Sterility Method of DP


Sterility testing is performed on the DP at (b) (4). Acceptance criteria of 'No Growth Detected' must be met for the lot release of SRP-9001.

Method:

(b) (4)

(b) (4)



Conclusion:

The method suitability tests were 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.