



DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To: STN125846/0

From: Tao Pan, Ph.D., CBER/OCBQ/DBSQC/LAC

Through: Kenneth S. Phillips, Ph.D., Chief, CBER/OCBQ/DBSQC/LAC
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Product: WASKYRA (etuvetidigene autotemcel)

Applicant: Fondazione Telethon ETS

Subject: Analytical Methods for the Lot Release of Wiskott Aldrich Syndrome Lentiviral Vector (WAS LVV) and Drug Product (DP)

Recommendation: Acceptable

Summary:

The following analytical methods used for lot release of WAS LVV, a critical component for WASKYRA manufacturing, and WASKYRA DP from Fondazione Telethon, and the associated validations and qualifications, were reviewed:

(b) (4)

5. Appearance (DP).

Conclusion: The analytical methods and their validations/qualifications reviewed for WAS LVV and WASKYRA DP, were found to be adequate for their intended use.

Documents Reviewed

Information in sections of the original submission that describe control of DS (3.2.S.4) and DP (3.2.P.5.), including descriptions of the specifications, analytical procedures and validation of these analytical procedures were reviewed.

Background:

WASKYRA DP is a cryopreserved dispersion for infusion of autologous CD34+ that contains hematopoietic stem and progenitor cells transduced ex vivo using WAS LVV; it is intended for the treatment of Wiskott-Aldrich Syndrome, a rare X-linked primary immune deficiency caused by mutations in the Wiskott-Aldrich syndrome protein that only expresses in hematopoietic cells and regulates actin polymerization.



Wiskott Aldrich Syndrome Lentiviral Vector (WAS LVV) is a liquid suspension of recombinant replication-incompetent self-inactivating HIV-1-based lentiviral vector that has been modified to carry the human Wiskott Aldrich Syndrome (WAS) cDNA sequence; it is used to transduce enriched autologous CD34+ ex vivo, and therefore, a critical component for the manufacturing of WASKYRA.

(b) (4)



2 pages have been determined to be not releasable: (b)(4)

(b) (4)

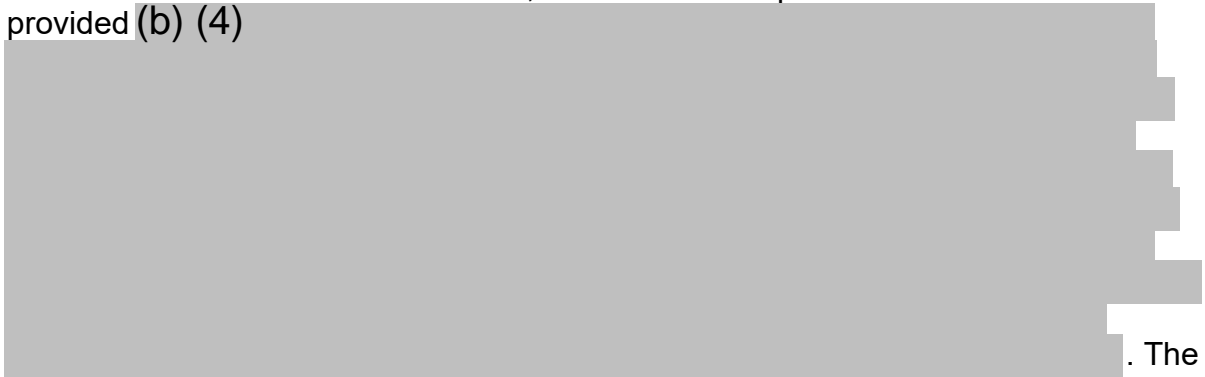


5. Appearance (DP)

The appearance of WASKYRA DP is determined by visual inspection; the specification for release is: “a cloudy to clear, colorless to yellow or pink dispersion of cells”. The method is performed for DP release at AGC Biologics S.p.A., Bresso, Italy.

Method:

Although the appearance of the DP was indicated to be determined by visual inspection for release, no detailed description of the method was provided; an information request (IR) was submitted on March 26, 2025 to seek additional information, and a response to the IR (#10) was received on April 11, 2025 in Amendment 0.10. In the amendment, a detailed description of the method was provided (b) (4)



. The provided description of the method is adequate with details on inspection procedures, result reporting and analyst qualification.

Method Verification:

No verification data were provided in the BLA, and an IR was submitted to seek additional information. In the response to the IR in Amendment 0.10, the sponsor stated that the appearance was not part of the release panel of the clinical lots and only added to the proposed commercial lots; however, all clinical DP lots underwent a visual inspection (b) (4) and were reported as “Pass”, and the result was consistent with the proposed specification of “a cloudy to clear, colorless to yellow or pink dispersion of cells”.

Conclusion:

Based on information provided, the appearance method has been verified for its intended use of release testing of the DP.