



DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To: The file: STN 125846/0

From: Claire H. Wernly, Ph.D.
Laboratory of Microbiology, *In-Vivo* Testing and Standards (LMIVTS)
Division of Biological Standards and Quality Control (DBSQC)

Through Maryna Eichelberger, Ph.D., Director, DBSQC
James L. Kenney, D.Sc., Chief, LMIVTS

Applicant: Fondazione Telethon ETS (Telethon).

Subject: Review of Sterility, Endotoxin and Mycoplasma Analytical Methods used for WASKYRA (etuvetidigene autotemcel).

Recommendation: Approval with Post Marketing Commitment (PMC)

Executive Summary:

The sterility, endotoxin and mycoplasma analytical methods used for testing and release of WASKYRA (etuvetidigene autotemcel) and the associated analytic method qualifications, were reviewed. The sterility and endotoxin assays were adequately described and shown to be suitable for their intended purpose. The mycoplasma analytical method reviewed for the WASKYRA drug product (DP) was found to be inadequate for its intended use in its current form. The additional validation data provided in the PMC will be used to complete the review and make a final determination on the adequacy of the method.

Conclusion: The sterility and endotoxin analytical methods and their qualifications reviewed for WASKYRA (etuvetidigene autotemcel) drug substance and drug product were found to be adequate for their intended use. The mycoplasma analytical method reviewed for WASKYRA drug product was found to be inadequate for its intended use in its current form. Additional validation data will be provided in the form of a PMC and will be used to complete the review and make a final determination on the adequacy of the method. FTE's post marketing commitment received on June 20, 2025 (Amendment #19), commits to perform a comparability study as part of the WASKYRA drug product (b) (4) mycoplasma assay as required by 21 CFR 610.9. The final validation study report will be submitted as a "Post marketing Commitment - Final Study Report" by September 30, 2026.

Documents Reviewed

Information in sections of the original submission that describe control of Drug Substance (DS) 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 qualifications of these analytical procedures were reviewed. In addition, the responses to CBER's Information Requests (IRs) received on April 21, 2025 (Amendment #12), June 20, 2025 (Amendment #19), September 10, 2025 (Amendment # 25), and November 10, 2025 (Amendment # 28), were also reviewed.

Background:

Fondazione Telethon ETS submitted BLA 125846/0 on January 10, 2025, WASKYRA (etuvetidigene autotemcel), an autologous CD34+ cell enriched population containing hematopoietic stem cells (HSCs) transduced with a non-replicating Lentiviral vector (LVV), referred to as TLT003 WAS LVV, encoding the human Wiskott-Aldrich syndrome (WAS) gene.

The drug substance (DS) is (b) (4)

The DP is the DS suspended in cryopreservation medium containing 5% dimethyl sulfoxide (DMSO), 7% HSA and 0.9% sterile saline. WASKYRA is supplied frozen in 50 mL ethyl vinyl acetate bags where each bag contains approximately 2×10^6 cells/mL suspended in 10 -20 mL of the cryopreservation medium. WASKYRA is administered through intravenous (IV) infusion after thawing.

This review focuses on the qualification of the sterility, endotoxin and mycoplasma tests as performed on the (b) (4) DP, to indicate if the product matrix is suitable for testing using the intended test method.

1. Sterility Test on (b) (4) DP



Introduction

This test is performed on (b) (4) DP at AGC Biologics S.p.A. (AGC) Bresso site in Milan, Italy. Specification of 'No Growth' must be met for lot release.

Review of Methods

(b) (4)



(b) (4)



The methods are described in more detail below together with the tests performed to determine the suitability of the test methods for their intended use.


The original validation reports for sterility lacked sufficient information to complete the review. Therefore, IRs were sent requesting data and clarification to fulfill these deficiencies. Responses were received on April 21, 2025 (Amendment #12), June 20, 2025 (Amendment #19), September 10, 2025 (Amendment # 25), and November 10, 2025 (Amendment # 28), which were found acceptable and explained below.

(b) (4)



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

(b) (4)



2. Endotoxin test on (b) (4) DP





Introduction

This test is performed on (b) (4) DP at AGC Biologics S.p.A in Milan, Italy

Specification of (b) (4) must be met for lot release of (b) (4) DP (b) (4)

Review of Methods

(b) (4)



(b) (4)

Conclusion

AGC Biologics S.p.A submitted bacterial endotoxin concentration results from DP lots, and all were within their proposed release specification (i.e., (b) (4)). After review of the (b) (4) test method, this reviewer concludes the test methods were performed and compliant with (b) (4)

3. Mycoplasma test on (b) (4) DP

Introduction

This test is performed on the (b) (4) DP at AGC Biologics S.p.A in Milan, Italy. Acceptance criteria of 'none detected' must be met for lot release.

Review of Methods

(b) (4)

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

(b) (4)

Conclusion

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

The mycoplasma analytical method reviewed for the WASKYRA DP was found to be inadequate for its intended use in its current form. Additional validation data will be provided in the form of a PMC and will be used to complete the review and make a final determination on the adequacy of the method. FTE's post marketing commitment received on June 20, 2025 (Amendment #19), commits to perform a comparability study as part of the WASKYRA drug product (b) (4) mycoplasma assay as required by 21 CFR 610.9. The final validation study report will be submitted as a "Post marketing Commitment - Final Study Report" by September 30, 2026.