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DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To: The file: STN 125874/0

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Applicant: Regeneron Pharmaceuticals, Inc. (Regeneron)

Subject: Review of (b) (4), Endotoxin and Sterility Analytical
Methods used for OTARMENI (lunsotogene parvec-cwha)

Recommendation: Approval

Executive Summary

The (b) (4), endotoxin, and sterility analytical methods used for testing and release of OTARMENI and the associated analytic method qualifications, were reviewed. The analytical methods were adequately described and shown to be suitable for their intended purpose.

Conclusion

The (b) (4), endotoxin, and sterility analytical methods and their qualifications reviewed for OTARMENI (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 Drug Substance (DS) and Drug Product (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 November 20, 2025 (Amendment 5), December 3, 2025 (Amendment 9), December 8, 2025 (Amendment 11), and January 16, 2026 (Amendment 32) were also reviewed.

Background

On November 6, 2025, Regeneron submitted a rolling Biologics License Application (BLA) under the FDA's Commissioner's National Priority Voucher (CNPV) Program for DB-OTO. The final module of the rolling submission was received on December 23, 2025. The product was initially proposed under the proprietary name DB-OTO (lunsotogene parvec). The proprietary name was subsequently revised to OTARMENI (lunsotogene parvec-cwha) and was approved by the Advertising and Promotional Labeling Branch (APLB) on January 30, 2026.

OTARMENI is an adeno-associated virus (AAV) vector-based gene therapy for the treatment of patients with hearing loss associated with biallelic pathogenic variants in the OTOF gene. It is supplied as a sterile suspension for intracochlear infusion. Each single-dose vial contains a nominal concentration of 3.0×10^{13} vector genomes (vg)/mL and provides an extractable volume of 0.63 mL. This review focuses on the qualification of the (b) (4), sterility, and endotoxin as performed on the (b) (4) final DP, to indicate the methods are suitable their intended use.

1. (b) (4)

(b) (4)

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(b) (4)

(b) (4)

3. Endotoxin Method (b) (4) DP)

Introduction

Endotoxin testing for OTARMENI (b) (4) DP is performed at (b) (4)
(b) (4) Specifications of (b) (4) DP must be met for release of
OTARMENI.

Review of Method

(b) (4)

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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. Sterility Method (DP)

Introduction

Sterility testing is performed on OTARMENI DP at contract testing laboratory, (b) (4). Specification of 'No Growth Detected' must be met for lot release.

Review of Method

(b) (4)

. The method is described in more detail below together with the tests that were performed to determine suitability of the test method.




In original sterility test qualification reports, CBER found issues with the Sponsor's sterility testing method. Sponsor used (b) (4) which does not meet our expectations or the generally recommended (b) (4) to provide optimal assay sensitivity. Therefore, IRs were sent requesting clarification and requalification of sterility assay. Responses were received on November 20, 2025 (Amendment 5), December 3, 2025 (Amendment 9), December 8, 2025 (Amendment 11), and January 16, 2026 (Amendment 32), which were found acceptable and explained below.

Sterility Test Qualification for DP


(b) (4) qualified their (b) (4) sterility method using OTARMENI DP by performing (b) (4) qualification studies to determine if the method is suitable the actual conditions of use. The test was performed using (b) (4)

(b) (4)

(b) (4)



Regeneron agreed to CBER's requests and submitted a requalification report inclusion of (b) (4)



CBER reviewed the requalification report and found the data acceptable.

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.