



DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To The file: STN 125816/0

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Product Avance Nerve Graft (processed nerve allograft)

Applicant Axogen Corporation (Axogen)

Subject Review of Endotoxin, Sterility, and Bioburden Analytical Methods used for
Avance Nerve Graft

Recommendation: Approval

Executive Summary

The bacterial endotoxin analytical method used for testing and release of Avance Nerve Graft® drug product (DP), the sterility method suitability test performed in accordance with (b) (4) during terminal sterilization validations for sterility release test as per (b) (4) control bioburden, and the associated analytic method qualifications, were reviewed. The assays were adequately described and shown to be suitable for their intended purpose.

Conclusion: The analytical methods and their qualifications reviewed for Avance Nerve Graft (b) (4) DP 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.2.4 and 3.2.P.5, respectively), including descriptions of their specifications and method were reviewed. In addition, responses to CBER's information requests (IRs) received on December 26, 2024 (Amendment #13), January 08, 2025 (Amendment #14; including a direct response from (b) (4) contract lab to RPM on January 6, 2025,

regarding 'sterility testing procedure, Q08-WI-002709', and April 17, 2025 (Amendment #33), were also reviewed as mentioned below.

Background

On July 31, 2024, Axogen submitted this BLA, for Avance Nerve Graft, a regenerative peripheral scaffold indicated for the treatment of peripheral nerve functional deficits. Avance Nerve Graft is a sterile single use only surgical implant specifically designed for use in cases where a peripheral nerve deficit requires repair. It is available in 16 combinations of diameters (1 to 5 mm) and lengths (15 to 70 mm).

Avance Nerve Graft is a decellularized and sterilized extracellular matrix (ECM) derived from human peripheral nerve tissue. The (b) (4) is manufactured using the Avance processing method that starts with using decellularized nerve tissue, removes axonal-growth inhibiting components, and clears the cellular and non-cellular debris from the nerve tissue, while preserving the ECM structure and bioactive laminin of the human peripheral nerve. The (b) (4) manufacturing process is a (b) (4) process that starts with (b) (4) of the starting material and ends with (b) (4) until DP manufacturing continues. (b) (4) DP and is packaged into a sterile barrier clamshell package, with a secondary packaging consists of two pouches, a sealed sterile Tyvek-poly pouch within a sealed foil poly pouch. The foil pouch is placed in a tertiary package, which is the commercial carton that is placed in a freezer for storage.

The proposed release specification for sterility test is terminal sterilization via (b) (4) with a dose range defined by sterilization validation in accordance with (b) (4). Neetu Dahiya - in CBER's OCBQ's Division of Manufacturing and Product Quality (DMPQ) - will review sterility by the terminal sterilization for Avance Nerve Graft DP. Sterility testing per (b) (4) is performed during sterilization validations, sterilization dose audits, and stability studies.





This review focuses on qualifications of the (b) (4) bioburden, bacterial endotoxin, and sterility tests to determine if these methods are suitable for testing the Avance Nerve Graft IPC (b) (4) DP under the actual conditions of use. The sterility test reviewed is performed during terminal sterilization validations, terminal sterilization dose audits, and for stability studies.

1. (b) (4) Bioburden Test

Introduction

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(b) (4)



2. Endotoxin (DP)

Introduction

(b) (4) bacterial endotoxin testing (b) (4) for processed nerve allograft is performed at APC (b) (4). The acceptance criteria of (b) (4) must be met for release of Processed Nerve Allograft DP. Note: The endotoxin limit of (b) (4) /graft is converted to (b) (4) by

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(b) (4)

DP acceptable.

Conclusion

The method suitability test was performed and compliant with (b) (4) and the test results indicate there is no product interference from Processed Nerve Allograft DP samples. Therefore, CBER determined their (b) (4) test method is appropriate under the actual conditions of use.

3. Sterility (DP)


Introduction

The proposed release specification for sterility test is terminal sterilization via (b) (4) with a dose range defined by sterilization validation in accordance with (b) (4). Acceptance criteria of 'Meets the requirements of parametric release' must be met for the lot release of Processed Nerve Allograft DP (the proposed release specification for sterility is (b) (4)). Neetu Dahiya - in CBER's OCBQ's Division of Manufacturing and Product Quality - will review the terminal sterilization sterility testing for Processed Nerve Allograft DP.

The compendial sterility test method is performed by (b) (4) in accordance with (b) (4) to confirm terminal sterilization and used for DP stability studies. Sterility testing for Processed Nerve Allograft DP is performed at (b) (4) or contract testing facilities (b) (4). DBSQC reviews sterility method suitability study determines if this method is suitable for testing the Processed Nerve Allograft DP to confirm terminal sterilization under the actual conditions of use.

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(b) (4)

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Conclusion

The method suitability tests were performed and compliant with (b) (4) and the test results indicate there is no product interference from Processed Nerve Allograft DP, thus indicating the (b) (4) sterility test method is appropriate under the actual conditions of use at (b) (4) sites.