



Our STN: BL 125816/0

**LATE-CYCLE
MEETING MEMORANDUM**

Axogen Corporation
Attention: Jesse Bishop
13631 Progress Boulevard, Suite 400
Alachua, FL 32615

Dear Jesse Bishop:

Attached is a copy of the memorandum summarizing your May 21, 2025 Late-Cycle Meeting with CBER. This memorandum constitutes the official record of the meeting. If your understanding of the meeting outcomes differs from those expressed in this summary, it is your responsibility to communicate with CBER in writing as soon as possible.

Please include a reference to the appropriate Submission Tracking Number (STN) in future submissions related to the subject product.

If you have any questions, please contact Eden Chane at 202-441-8882.

Sincerely,

Beatrice Kallungal, MS
Director
Division of Review Management and Regulatory Review 1
Office of Review Management and Regulatory Review
Office of Therapeutic Products
Center for Biologics Evaluation and Research

Late-Cycle Meeting Summary

Meeting Date and Time: May 21, 2025 From 2:00 PM- 3:00 PM
Meeting Location: WO22-1313
Application Number: BL 125816/0
Product Name: Avance Nerve Graft (Processed Nerve Allograft)
Proposed Indications: Avance Nerve Graft (processed nerve allograft) is a regenerative peripheral nerve scaffold indicated for the treatment of peripheral nerve functional deficits
Applicant Name: Axogen Corporation
Meeting Chair: Wen (Aaron) Seeto, PhD
RPM: Eden Chane

FDA ATTENDEES

Afsah Amin, MD, MPH, CBER/OTP
Rachael Anatol, PhD, CBER/OTP
Srinivas Ayyala, MD, CBER/OBPV/DPV
Rabia Ballica, PhD, CBER/OCBQ/DMPQ
Holly Brevig, PhD, CBER/OCBQ/DMPQ
Kathyleen Jones, PhD, CBER/OCBQ/DMPQ
Eden Chane, MS, CBER/OTP/ORMRR
Maureen DeMar, RN, BSN, CBER/OCBQ/DMPQ
Neetu Dahiya, PhD, CBER/OCBQ/DMPQ/MRB1
Adriane Fisher, MPH, MBA, CBER/OTP/ORMRR
Beatrice Kallungal, MS, CBER/OTP/ORMRR
Tyree Newman, MDiv, CBER/OTP/ORMRR
Miriam Ngundi, PhD, CBER/CBQ/DMPQ
Steven Oh, PhD, CBER/OTP/OCTHT
Tanbin Rahman, PhD, CBER/OBPV/DB/TEB
Helen Sansone, CBER/OTP/ORMRR
Wen (Aaron) Seeto, PhD, CBER/OTP/OCTHT
Rosa Sherafat-Kazemzadeh, MD, CBER/OTP/OCE/DCEGM
Jin Sung Hong, PhD, CBER/OTP/OCTHT
Zehra Tosun, PhD, CBER/OTP/OCTHT
Harry Houghton, MS, CBER/OBPV/DB

APPLICANT ATTENDEES

Stacy Arnold Vice President of Product Development and Clinical Research
Marc Began Executive Vice President & General Counsel
Jesse Bishop, Vice President, Regulatory
Xavier Cortez, Director, Quality Engineering
Erick DeVinney, Chief Innovation Officer
Ivica Ducic, MD, PhD, Chief Medical Officer

Zana Dupee Director, Regulatory Affairs
Mark Friedman, PhD, Senior Advisor, Biologics
Al Jacks, Vice President, Quality
Craig Swandal, Vice President, Operations
Elysha Liles Manager, Manufacturing/Process Engineering
Kyle Icke, PhD, Director, Clinical Science

(b) (4)

Carter McCain, Director, Quality Systems Compliance
Dolores Valente, Sr. Director, Deputy General Counsel
Jonathan White, Manager, Regulatory Affairs
Pavan Jhutti, Senior Manager, Regulatory Affairs
Rachel Moreno-Williams, Director, Clinical Policy

(b) (4)

BACKGROUND

BLA 125816 was submitted on September 5, 2024, for Avance Nerve Graft (Processed Nerve Allograft).

Proposed indication: Avance Nerve Graft (processed nerve allograft) is a regenerative peripheral nerve scaffold indicated for the treatment of peripheral nerve functional deficits.

PDUFA goal date: September 5, 2025

In preparation for this meeting, FDA issued the Late-Cycle Meeting Materials on May 9, 2025.

DISCUSSION

1. Discussion of Substantive Review Issues

Chemistry Manufacturing and Controls (CMC)

- Redistribution of returned drug products
- Impurity profile of the drug product

Meeting Discussion:

Redistribution of returned drug products: Axogen confirmed that they will not re-distribute returned product. The process to re-distribute returned product has been removed from the BLA and the returned material procedure will not be implemented at Axogen Processing Center (APC). Returned product will be re-purposed for research or educational purposes. FDA stated that the Applicant should submit this change through an amendment to the BLA.

Impurity profile of the drug product: Axogen has developed multiple risk assessments associated with the risk of visible (b) (4). Axogen has also presented ongoing developments, in addition to the current controls in place, to reduce visible (b) (4) in the drug product. As some of the improvements will be detailed in the 483 response, FDA commented that they will review Axogen's 483 response and follow up with information request, as needed, to address the issue.

Division of Manufacturing and Product Quality (DMPQ)

- Sterilization process
- Integrity of the sterile barrier system of the drug product, Avance

Meeting Discussion:

The FDA commented that bioburden is evaluated as (b) (4) controls for the Avance (b) (4) manufacturing process. As a justification for (b) (4) bioburden samples, you have referenced Section 5.4.1 in Association for the (b) (4)

(b) (4) that indicates the shipping, storage, and sampling conditions should be designed to minimize conditions, which are conducive to microbial growth on the biologic/tissue. However, it does not mean that bioburden test samples can be stored under conditions that could impact the viability of microorganisms that are already present in the sample.

(b) (4) As your product is (b) (4) released, bioburden is the critical parameter for the sterilization of the Avance product. The FDA's expectation is that microbial control samples e.g., bioburden and sterility are stored between (b) (4) and tested within (b) (4). The firm commented that the sample storage conditions are representative of manufacturing process and the bioburden that is tested on the (b) (4) samples is presented to the sterilization process. In response, the FDA emphasized that supporting data for evaluating the impact of proposed sample

storage conditions for microbial controls is lacking. The (b) (4) bioburden samples are not suitable for bioburden testing as (b) (4) control of the Avance product manufacturing. Upon further conversations with FDA experts following the meeting, FDA confirmed that due to the parametric release and lack of a controlled environment, we recommend also (or at a minimum) performing bioburden under worst case conditions, which is on the (b) (4) sample.

In response to the firm's justification on the loading configuration for sterilization of the Avance product, the FDA commented that we are currently in the process of reviewing the information request (IR) response received on May 19, 2025, on loading configuration for sterilization validation and will communicate through IRs/informal telecons if additional information is needed.

In response to the proposed container closure integrity testing, the FDA commented that we acknowledge that in your IR response you are proposing a (b) (4) method in alignment with (b) (4) for evaluating the container closure integrity of the Avance drug product. However, the proposed method and timelines to provide data to support integrity of the container closure system and transportation validations are still under review. Please note that the proposed submission dates for the validation reports are close to the action due date of the BLA. We are currently in the process of reviewing the IR response received on May 16, 2025, and will communicate through IRs/informal telecons if additional information is needed. The firm requested to provide feedback on the CCIT method as early as possible, and in response the FDA commented that feedback will be provided as soon as the review of IR response is completed.

2. Discussion of Established Pharmacologic Class

Meeting Discussion:

No discussion during the meeting

3. Additional Applicant Data

Meeting Discussion:

No discussion during the meeting

4. Information Requests (IR)

Meeting Discussion:

Response to all IRs are received and pending review.

No discussion during the meeting

5. Risk Management Actions (e.g., REMS, the ability of adverse event reporting and CBER's Sentinel Program to provide sufficient information about product risk)

There is no anticipation of a REMS at this time.

Meeting Discussion:

No discussion during the meeting.

6. Postmarketing Requirements/Postmarketing Commitments
There is no PMR and PMC identified at this time

Meeting Discussion:

No discussion during the meeting.

7. Major Labeling Issues
Labeling review is ongoing

Meeting Discussion:

No discussion during the meeting.

8. Review Plans
Review of the BLA is on-going. We will continue sending IRs as necessary to get clarification on any submitted information.
- Labeling Target Date: August 6, 2025
 - PMC Target Date: August 6, 2025
 - PDUFA Date: September 5, 2025

Meeting Discussion:

No discussion during the meeting

9. Applicant Questions

Q1. Can FDA provide an update on the status on the Revised (b) (4) Source Replenishment Protocol (PROT-0919)?

Meeting Discussion:

The FDA commented that PROT-0919-R01 was received on March 28, 2025. The Agency has reviewed the protocol and do not have additional comments to provide at this time.

Q2. Has FDA considered the Administration Technique Guide as presented in 1.14.1.3 (Draft Labeling Text) as part of its preliminary review of prescribing information?

In reviewing other precedents (e.g. Rethymic) we see that some of the information contained in our Administration Technique Guide may be better incorporated in section 2 of the prescribing information.

Meeting Discussion:

The review of label is ongoing, and related comments will be communicated during the planned labeling negotiations. Please note that information needed for safe and effective administration of the product, including surgical steps for Avance implantation should be included in Section 2 of USPI.

Q3. If time allows, can FDA provide the status of the following open waiver requests?

- a. Categorical exclusion from an Environmental Assessment per 21 CFR Part 25.31
- b. Sterility Testing per 21 CFR 610.12
- c. Reserve Samples inspection per 21 CFR 211.170
- d. Drug Supply Chain Security Act (DSCSA) Exemption

Meeting Discussion:

The FDA commented that the waiver requests are still under review, and an information request will be sent if there are additional questions. For waiver request item 'b', the FDA commented that the team is currently in the process of reviewing the IR response received on May 19, 2025, for validation of the sterilization process for the Avance drug product. The team do not have additional comments to provide at this time as this request is associated with the (b) (4) release and additional information is needed to support (b) (4) release. The FDA referred to additional information requested for sterilization validation discussed under review issues.

10. Wrap-up and Action Items

The late cycle meeting summary will be sent by Friday June 20, 2025

Meeting Discussion:

No discussion during the meeting

This application has not yet been fully reviewed by the signatory authorities, Division Directors and Review Committee Chair and therefore, this meeting did not address the final regulatory decision for the application.