

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT OFFICE ADDRESS AND PHONE NUMBER CBER/OCBQ/Division of Manufacturing and Product Quality 10903 New Hampshire Avenue, Silver Spring, MD 20993 Lead Insp.: Miriam Ngundi Telephone: 240-402-9774 Industry Information: www.fda.gov/oc/industry	DATE(S) OF INSPECTION April 23-25 and 28-29, 2025
	FEI NUMBER 3023488176

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

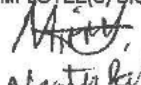
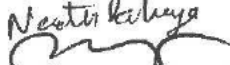
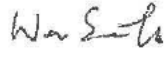
TO: Mike Hoff, VP, Manufacturing

FIRM NAME Axogen Corporation	STREET ADDRESS 913 Industrial Park Drive
CITY, STATE AND ZIP CODE Vandalia, OH 45377	TYPE OF ESTABLISHMENT INSPECTED Drug substance and drug product manufacturer

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS; AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM I(WE) OBSERVED:

1. Procedures describing the warehousing of AVANCE final product, printed product labels, and retain samples are not established. Specifically:
 - a. Areas where AVANCE final product is stored are not controlled. All personnel including contractors for cleaning services with access to the controlled not classified (CNC) areas have access to Rooms (b) (4) and (b) (4), where AVANCE final product are stored in unlocked freezers.
 - b. Access to the storage area for labels is not limited to authorized personnel. Specifically, printed serial barcode labels are stored unsecured in Rooms (b) (4) which are accessible to all personnel including contractors for cleaning services.
 - c. There is no documentation including sample identification or location of the inventory of (b) (4) (b) (4) samples for the potency assay.
2. Environmental monitoring program is deficient to ensure classified environments. For example:
 - a. Monitoring of viable and nonviable particulates under static and dynamic conditions during the environmental monitoring performance qualification (EMPQ) of ISO classified manufacturing areas was inadequate to support routine environmental monitoring. Specifically, the following monitoring was not performed:
 - i. Microbiological surface monitoring of ISO 8, ISO 8, and ISO 8 classified areas under static condition was performed (b) (4) to prevent recovery of microorganisms present.
 - ii. Monitoring of nonviable particles in ISO 8 classified areas under static and dynamic conditions, and in ISO 8 classified areas under dynamic conditions was not performed.
 - iii. Microbiological active air monitoring in ISO 8 classified areas under static and dynamic conditions, and in ISO 8 and ISO 8 classified areas under dynamic conditions was not performed. Further, passive air monitoring using microbiological settling plates in ISO 8 classified areas under static conditions, and ISO 8 and ISO 8 classified under static and dynamic conditions was not performed. Additionally, microbiological surface monitoring was not performed in ISO 8, ISO 8, and ISO 8 classified areas

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under dynamic conditions.

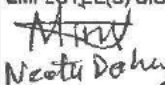
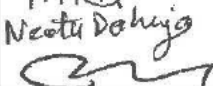
b. Routine environmental monitoring is inadequately established in classified areas. Specifically:

- i. Monitoring of nonviable particles is not performed in ISO ^{(b) (4)} and ISO ^{(b) (4)} classified areas, where ^{(b) (4)} and ^{(b) (4)} packaging manufacturing operations occur.
- ii. Microbiological active air and surface monitoring is not performed in ISO ^{(b) (4)}, ISO ^{(b) (4)}, and ISO ^{(b) (4)} classified areas, where ^{(b) (4)} packaging and labeling manufacturing operations occur.

3. Manufacturing building used in the manufacture of AVANCE does not have the adequate controls to prevent contamination. For example:

- a. There is no disinfectant efficacy study to support the use of ^{(b) (4)} which is approved for use as a routine ^{(b) (4)} disinfectant for ^{(b) (4)} per SOP-0540 R11 ^{(b) (4)} Environmental and ^{(b) (4)} Equipment Cleaning and Disinfection Program." Specifically, in Reports RPT-0514 R00 "Summary for the Disinfectant Efficacy Testing for the ^{(b) (4)} ^{(b) (4)}" and RPT-0573 "Summary Report for the Axogen Processing Center Disinfectant Study for Cleanroom Surfaces," the effectiveness of ^{(b) (4)} was not assessed against ^{(b) (4)}, which is commonly used to hold ^{(b) (4)} materials that are ^{(b) (4)} into classified areas.
- b. Written procedures are not established to disinfect materials when ^{(b) (4)} materials from ^{(b) (4)} ^{(b) (4)} classified areas. For example, on April 28, 2025, your firm explained that ^{(b) (4)} manufacturing materials used for manufacturing in ISO ^{(b) (4)} are disinfected with ^{(b) (4)} ^{(b) (4)}
- c. The residual level of ^{(b) (4)} on sterilized equipment was not established nor monitored.
- d. The "shelf-life post-sterilization" for equipment sterilized using ^{(b) (4)} and an ^{(b) (4)} is not supported. In report RPT-1045 R00 "Summary Report for Performance Qualification for ^{(b) (4)}," you claim a shelf-life post-sterilization based on the manufacturer's instruction ^{(b) (4)} for equipment in a ^{(b) (4)} ^{(b) (4)} respectively. However, there is no data to support the equipment maintains a level of cleanliness to prevent the introduction of microbial contaminants to the manufacturing process after the hold.

4. Written procedures for production and process control are inadequate or not established to assure that the AVANCE drug product has the identity, strength, quality, and purity that it purports or is represented to possess.

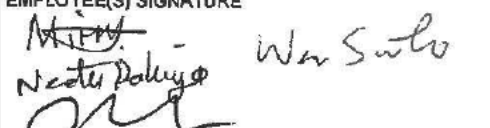
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For example:

- a. On April 25, 2025, it was observed that operators who perform packaging, labeling, sealing, and visual inspection of Batch (b) (4) had executed (b) (4) activities of drug substance to (b) (4) the nerve graft within the clamshell. However, the batch record (b) (4) lists the activities as only Tyvek and foil (b) (4). Additionally, SOP-0166 R07 "Package Assembly Visual Inspection and Testing" provides that (b) (4) can be performed due to defects on the seals of the Tyvek and foil pouches or presence of particulates. SOP-0166 R07 and (b) (4) do not permit (b) (4) to include (b) (4) of the nerve graft.
 - b. SOP-880 "Sizing, Inspection, and Packaging of Avance Drug Substance" Section 7.5^{(b) (4)} states (b) (4) (b) (4). However, deviation DEV-2024-0462 was initiated due to (b) (4) not placed inside BSC during packaging.
 - c. Procedure(s) describing the processing of returned drug product is not effective. Approved SOP-0943 R00 "(b) (4) Returned Material Procedure, Avance" and draft (b) (4)-0018 R00 "Avance RMA Visual Inspection Work Instruction" are not yet effective and not all personnel have been appointed and trained to perform the intended operation.
 - d. In step 7.5^{(b) (4)} of SOP-0880 R02 "Sizing, Inspection, and Packaging of Advance® Drug Substance", manufacturing operators are permitted to remove visible non-viable particulate contamination (b) (4) (b) (4) from the nerve graft after the graft has been placed into a clamshell (i.e., primary container closure) or to transfer the graft into a clean clamshell due to the presence of particulates in the clamshell at the manufacturing operators' discretion. However, such activities are not documented in drug substance batch record FORM-0861 R03 "Avance Nerve Graft (Avance) Drug Substance Master Batch Record."
5. Laboratory controls are not adequately established and do not include scientifically sound test procedures and sampling plans designed to assure that AVANCE drug product conform to appropriate standards of identity, strength, quality, and purity. Specifically:
- a. The number of qualified personnel to perform drug product potency release testing is inadequate. Specifically, there is only (b) (4) personnel qualified to perform the potency assay of AVANCE drug product.
 - b. (b) (4) is inadequate. For example, (b) (4) using the (b) (4) is not performed on the sterilized bulk drug product or returned drug product after receipt at your facility.

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6. Investigations into pest control deviations are deficient. Specifically, twelve incidences of pest sightings were observed in controlled areas since 01 January 2025, four of which were in classified areas, and no CAPAs were opened prior to 23 April 2025. Corrective actions were implemented from DEV-2024-1511, which was opened on 27 November 2024. However, the corrective actions were not effective as five pest sightings have been identified in (b) (4) since 26 March 2025.

7. Deviation management is inadequate to demonstrate quality oversight of the manufacturing process. For example, the process to document and report deviations per (b) (4)-0013 R23 "Deviation Procedure" lacks the assurance that all deviations are recorded, because only select individuals who are trained in the deviation process can initiate deviations. Deviations cannot be initiated directly by manufacturing or laboratory staff who are not trained to the deviation process even if staff may be most knowledgeable about a specific deviation.

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Miriam Ngundi
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EMPLOYEE(S) NAME AND TITLE (Print or Type)

Miriam Ngundi, Lead Inspector, CSO
Neetu Dahiya, Biological Reviewer
Wen Seeto, Staff fellow
Jin Sung Hong, Lead Biologist

DATE ISSUED

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgement, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."