DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
New England District Office 109 Holton Street, Winchester, MA, 01890 781-587-7500 Industry Information: www.fda.gov/oc/industry	3/18/2026-4/9/20269
	FEI NUMBER 1220423

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Quentin Seemuller - Site Head for the MA BioCampus

FIRM NAME	STREET ADDRESS
Genzyme Corporation	8, 31,45,49,51,55,68,74,76,80 New York Ave
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Framingham, MA 01701-8861	Biologic drug substance 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:

OBSERVATION 1
Release of drug substance with documented particle contamination.

Specifically,

Your firm has released (b) (4) and (b) (4) drug substance lots with documented (b)(4) particle contamination as detected in appearance testing. For example, your firm opened laboratory investigations QE-109224 and QE-106364 in November and December 2024 for OOS appearance results for (b) (4) and (b) (4) drug substance lots (b) (4), and (b) (4), during release and retain sample appearance testing. The particles were identified as (b)(4) The (b) (4) release specification for appearance is (b)(4) Despite the OOS appearance results, your firm concluded that the (b)(4) particulate/particles were of no impact to the process or product as they are intrinsic to the manufacturing process and that subsequent manufacturing steps would remove the contamination. Your firm released the impacted lots despite confirming a manufacturing root cause of improperly set up (b)(4) that shed the (b)(4) particles into the manufacturing process.

Release of (b) (4) and (b) (4) drug substance lots with appearance test results documenting (b)(4) particle contamination was noted during the 2024 FDA inspection (6/12/2024-7/9/2024).

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OBSERVATION 2
Failure to adequately investigate significant deviations regarding bulk drug substance manufacture.

Specifically,

The following inadequate investigations were noted during the inspection:

• Your firm does not always follow your firm's (b)(4) and deviation process (QU-GOP-0000518 "Deviation Process Management") and "QU-SOP-0074684-Good Documentation Practices", when unexpected manufacturing events occur nor adequately investigate and remediate the issue(s) to prevent reoccurrence. For example, on 1March2026, during the (b)(4) process in preparation for (b) (4) lot (b) (4) bioreactor operations, manufacturing operators were unable to complete the (b)(4) step because the media would not (b) (4) (b)(4) as required per step QU-SOP-0080430 " (b)(4) Operation at (b)(4)", step 6.4.52. The (b)(4) devices require (b)(4) before they can be utilized for (b)(4) bioreactor operations for the (b) (4) drug substance. Instead of initiating a (b)(4) and deviation per QU-GOP-0000518, the firm left the (b)(4) overnight and the next dayshift resumed operations the following day. Your firm did not investigate why the (b)(4) step could not be completed on 1March2026. Additionally, the operators who performed the (b)(4) operations on 1March2026, did not contemporaneously sign for the (b)(4) steps they had completed in the batch record, and instead the dayshift on 2 March2026 signed that they had completed the (b)(4) step for the (b)(4). On 3/18/2026, I observed operators attempt to (b)(4) an (b)(4) unit in preparation for the manufacture of (b) (4) drug substance batch (b)(4). I observed that the operators were unable to complete the (b)(4) step because the media would not (b)(4) as required per step QU-SOP-0080430. A (b)(4) was called and deviation initiated. The root cause of the inability to (b)(4) the (b)(4) was due to the incorrect sequencing of (b)(4) removal from the (b)(4) unit (as described in QU-SOP-0080430) during (b)(4) operations, a process that your firm updated per change control CC-013836 in 2026.

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• Your firm does not adequately investigate when your cleaning verification program is not followed. For example, in January 2024, your firm documented failed cleaning verification testing for the (b) (4) column C3112060 for bioburden (result >200 CFU/10 mL, P. glucanolyticus, action specification (b)(4) mL). Per MABC-QU-SOP-0065841 "Cleaning Verification Procedure for Framingham Biologics and Biosurgery", the column was to be (b)(4). Instead, a (b) (4) run of the column was conducted and P. glucanolyticus was again recovered at 2 CFU/10 mL (below action specification (b)(4) mL). No additional remediation was performed and the column stored until use in March 2024, where (b)(4) (b) (4) (b) (4) lots were processed over the column. In September 2024, and October 2024, bioburden contamination of the associated (b) (4) and (b) (4) (b) (4) for lots (b) (4) and (b) (4) (P. glucanolyticus and other microorganisms) occurred as documented in QE-072568. While your firm rejected the directly impacted lots and conducted remediation activities for the (b) (4) and column, your firm failed to adequately investigate and holistically assess prior cleaning verification activities to ensure they were completed per your cleaning verification program.

• Since February 2024, your firm has opened 14 quality events (deviations and trend investigations) related to in-process control failures for the (b) (4) (b)(4) manufacturing process for cell viability (specification (b)(4) to include investigations opened in December 2025 and February 2026 (QE-1676923, QE-1686568, QE-1687770). Your firm has linked bioreactor performance to (b) (4) drug substance quality per QU-OPE-23832498 "Evaluation of process attributes with (b)(4) for (b) (4) " (impact on (b) (4), and (b) (4)). Your firm has attributed the cell viability in-process failures to the age of the (b)(4) bioreactor (b)(4) and the age of the film (b)(4)) utilized to manufacture the bioreactor (b) (4) contain the antioxidant (b)(4) , which can degrade after (b)(4) irradiation and over time leading to (b)(4) of a cytotoxic degradant (b)(4) into the process stream. Your firm halted (b) (4) manufacture in (b) (4) and conducted investigation QE-1676923 due to low cell viability of lot (b) (4) Your firm resumed (b) (4) manufacture in March 2026 with the interim control of controlling the age of the (b)(4) bioreactor (b)(4) and (b)(4) utilized in (b)(4) manufacture. Your interim control is inadequate in that it did not account for/evaluate other (b)(4) items (e.g., cell culture media (b)(4) that also contain (b)(4) which can potentially (b)(4) into the (b) (4) bioreactor posing a risk to the process.

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OBSERVATION 3
Failure to adequately re-qualify critical drug substance manufacturing equipment after movement and re-installation.

Specifically,

Your firm lacks adequate space to store the (b) (4) and (b) (4) (undergoing PPQ) (b)(4) purification equipment simultaneously in the Grade D suite 2 (b)(4) purification area. For example, due to the space limitation, the (b) (4) drug substance (b) (4) utilized for the (b) (4) chromatography (b) (4)) step is uninstalled and moved to an unclassified storage area when your firm manufactures Nexviazyme drug substance. Your firm moves the (b)(4) the Grade D suite (b) (4) area when (b) (4) drug substance production is (b)(4) Your firm is to conduct a clean in place (CIP) and cleaning verification (considered cleaning performance qualification) of the (b) (4) post installation. Your firm's program for movement and relocation of critical CGMP equipment is inadequate for the following reasons:

- In August 2024, your firm moved the (b) (4) into the suite (b) (4) (b)(4) area and conducted a CIP of the system, however, failed to perform cleaning verification. The subsequent two (b) (4) lots ((b) (4) and (b) (4)) produced with (b) (4) and the associated (b) (4) column had action level bioburden excursions and had to be rejected (Paenibacillus glucanolyticus and other microorganisms).

- MABC-QU-SOP-0016987 "Product Changeover at (b)(4) " and the associated work order tracking process for movement of the (b) (4) gives conflicting instructions on whether a post equipment move cleaning verification activity is required for GMP equipment.

Additionally, as of 4/3/2026, your firm has (b)(4) pieces of manufacturing equipment for the (b) (4) drug substance and (b)(4) pieces of manufacturing equipment for the (b) (4) drug substance (undergoing PPQ) that can be moved per MABC-QU-SOP-0016987, and it remains to be determined if prior equipment movement activities omitted required re-qualification actions.

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OBSERVATION 4
Failure to establish and follow adequate production control procedures.

Specifically,

A. Manufacturing operators do not follow procedure MABC-QU-SOP-0084522 "(b)(4)" during (b)(4) operations. For example, on 3/20/2026, I observed operators (b)(4) onto the (b)(4) using a (b)(4) in preparation of bioreactor operations for (b) (4) lot (b) (4). (b)(4) must be (b)(4) onto the (b)(4) and (b)(4) units aseptically and correctly to ensure that the bioreactor system remains sterile and contamination free. Prior to each (b)(4) event, operators are to clean the interior (b)(4) and bracket components of the (b)(4) with (b)(4) and (b)(4). I observed that the manufacturing operators failed to clean the (b)(4) brackets prior to the (b)(4) activities performed.

B. QU-SOP-0084643 "Gowning procedure for entry into aseptic processing area at (b)(4) ", is not followed by all employees. For example, on 27March2026, I observed the pre-use inspection of (b)(4) shipping bags for the filling of (b) (4) lot (b) (4) Secondary sterile gowning is required for the (b)(4) (b) (4) inspection and requires sterile sleeves and sterile gloves. Per QU-SOP-0084643, operators are to put on the sterile sleeves halfway, don sterile gloves, and then pull the sleeves all the way from the inside so as not to compromise the sterile gowning. The QA floor employee in the room, who was assisting the(b) (4) inspection, was observed to not follow the required sequence and fully don the sterile sleeves using non-sterile gloves.

C. MABC-QU-SOP-0065840 "Process Monitoring Procedure for Biologics Operations" is deficient as it does not outline timeframes for review and approval of statistical process data (continued process verification/CPV) conducted per MABC-QU-SOP-0065840. Additionally, statistical process review data for the (b) (4) and (b) (4) drug substance manufacturing processes are not reviewed and approved in a timely manner. For example, the last(b) (4) statistical process data review period was for (b) (4) manufacturing operations that occurred from 9July2024- 30January2025. The associated report (QU-OPE-2786314) evaluating the data from 9July2024- 30January2025, was not reviewed and approved until approximately five months later (27June2025).

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CAPA-691676 is open and pending regarding revision of your CPV program.

OBSERVATION 5
Drug substance manufacturing equipment is not cleaned and maintained appropriately.

Specifically,

On 30March2026, I inspected your firm's column packing area and noted the following deficiencies:
• Unknown white residue on the piping below the (b)(4) (b) (4) for the chromatography qualification (b) (4)(equipment ID(b) (4)). Your firm cleaned the residue on 30March2026 and observed the residue again on 31March2026, indicating a leak.

• Unknown brown residues/discoloration within (b) (4) chromatography hoses SP06-3200001 and PO6-3200003 (column inlet and drain hoses). The hoses were in clean status and in clean storage.

OBSERVATION 6
Specifically,

Failure to establish and follow adequate laboratory control mechanisms.

A. Your firm's inventory tracking of critical laboratory materials is inadequate. On 25March2026, I reviewed the critical materials inventory log sheet for the (b) (4) primary reference standard (b)(4) which documented that the (b)(4) vials were in freezer equipment ID# 70-QC-1046. (b)(4) is the(b) (4) primary reference standard utilized to qualify working reference standards utilized for drug substance release testing. The (b)(4) vials were not located within freezer equipment ID# 70-QC-1046 and instead located in freezer equipment ID# 70-QC-1046FB-5376. The inventory log sheet for (b)(4) was not updated when the material was moved and the associated log sheet procedure (QU-SOP-0067941 "QC Assay Controls, Standards and Critical Materials Inventory Management) is deficient in that it does not require material movements from different storage locations to be tracked and documented.

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B. Your firm's non-routine sample request procedure, QU-SOP-0033695 "Non-Routine Sample Request Procedure for Framingham Biologics", is inadequate in that the procedure does not include established timeframe requirements for completion of the various elements of the NRSR process (i.e., NRSR label reconciliation, NRSR batch record exception documentation, NRSR closure, and NRSR filing). The NRSR process is to obtain samples from GMP manufacturing processes which fall outside of pre-established sampling plans outlined in your firm's LIMS system. Additionally, your firm's review of your NRSR system during the inspection revealed instances of a batch record exception not being documented for taking an NRSR sample (NRSR# 25SR8015) and manufacturing not documenting how many NRSR sample labels were used and returned (NRSR # 25SR8119 and 25SR8120). Batch record exceptions and NRSR label sample reconciliation are required per QU-SOP-0033695.

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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."