DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10903 New Hampshire Ave, Bldg 71, Rm 5054 Silver Springs, MD 20993-0002 (240)402-9160	01/12/2026-01/20/2026
	FEI NUMBER 3003809840

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Cian O' Brien, Site Head

FIRM NAME	STREET ADDRESS
Genzyme Ireland Limited	Unit 701, Ida Industrial Park, Old Kilmeaden Road
CITY, STATE, ZIP CODE, COUNTRY Waterford, Co. WATERFORD, X91 TP27, Ireland	TYPE ESTABLISHMENT INSPECTED 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 WE OBSERVED:

OBSERVATION 1

Laboratory records are deficient in that they do not include a complete record of all data obtained during testing.

Specifically, deficiencies in documentation and data integrity were identified in environmental monitoring and (b) (4) testing records. The records and data for these quality control activities do not demonstrate adequate integrity controls and documentation practices.

A) Failing non-viable particulate testing data present in the history of (b) (4) Particle Counters is not investigated for product impact, documented as a part of the testing record, or otherwise evaluated. Instances of such findings are summarized as follows:

No.	Date	Controlled Form	Sampling Location	Official Documentation	Instrument Data	Acceptance Criteria for ≥0.5 µm particles	Discrepancy
		(b) (4)					
1	3-Jan-2025						Action level excursion not reported
2	3-Feb-2025						Action level excursion not reported
3	18-Aug-2025						Alert level excursion not reported
4	15-Jul-2025						Alert level excursion not reported
5	13-Sep-2025						Action level excursion not reported
6	27-Nov-2025						Alert level excursion not reported

*Initial, unreported result from (b) (4) testing events.

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Massoud Motamed, Investigator

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Note: All particle counts are reported as particles per cubic meter (particles/m³). Examples 3-6 involved (b) (4) testing events where only the (b) (4) result was reported on the controlled form, while the (b) (4) results showing excursions were not documented in official records.

B) The data present on (b) (4) Air Samplers used in active air monitoring does not support the conduct of the respective environmental monitoring, showing inconsistencies between documented sampling activities and actual instrument usage records. Examples are listed below:

No.	Date	Controlled Form	Air Samplers Used	Documentation Claims	Instrument Data Shows	Discrepancy
1	(b) (4)					Lack of accountability between active air monitor and environmental monitoring documentation
2						Lack of accountability between active air monitor and environmental monitoring documentation
3						Testing absent from instrument history
4						Testing absent from instrument history
5						Testing absent from instrument history

C) Failing (b) (4) testing is not investigated. Specifically, procedure (b) (4)-SOP-0071168 titled " (b) (4) Testing" Section 5.15 reads "If the (b) (4) fails a (b) (4) refer to (b) (4) SOP-0070985 'Deviations and Investigations', Process Engineering will raise a customer complaint. The investigation and root cause analysis along with the conclusive testing result must be referenced in the EBR." Despite the procedure, the testing history of the (b) (4) instruments indicate testing events where more than one failure was encountered, but no accompanying deviation was raised. Further, the electronic batch records fail to document the (b) (4) failures, and Altuviiio batches (b) (4) and (b) (4) have been released. These findings are tabulated below:

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Batch Number	Product	Number of Testing Failures	Deviation
(b) (4)	Altuviiio	(b) (4)	No
	Altuviiio		No
	(b) (4)		No
	Altuviiio		No
	(b) (4)		No
			No
	Altuviiio		No
	Thymoglobulin		No
	(b) (4)		No

D) Official records are inconsistent with Good Documentation Practices:

1) Your firm utilizes "Review Checklist" to unofficially document findings of Quality Control document reviews. The "Review Checklist" is subsequently (b) (4) Moreover, a review of the "Review Checklist" identified entries that were made non-contemporaneously that were not attributed as such. The "Review Checklist" pertaining to December 16, 2025 reads "'yes' not circled for Acceptance criteria" and "Sample results not entered." However, the corresponding record ((b) (4) -0115397) contains a circled 'yes' and incorporates the sample results without documentation that these entries are retrospective.

2) The logbooks documenting the entrance and exit times from the cleanrooms are inconsistent with the sampling times for environmental monitoring. Specifically, personnel conducting environmental monitoring are not documented as being present in the cleanroom at the times the sampling was conducted. For example, on October 13, 2025, environmental monitoring personnel are documented as being present in the cleanroom between (b) (4) however, environmental monitoring is documented as being conducted from (b) (4)

3) Your firm uses (b) (4) to instruct personnel to review/ revise records. On January 19, 2026, (b) (4) encompassing review comments were observed in on official documentation in the Quality Control area. Your procedure (b) (4) -0034155 entitled "Data Integrity" states "The use of (b) (4) is not permitted in GMP areas."

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OBSERVATION 2

The responsibilities and procedures applicable to the quality control unit are not in writing and fully followed.

Specifically, your procedure requires a change control to be issued for implementing changes. This requirement is delineated in SOP (b) (4) -0000514 titled "Change Control Management". However, several examples were found where a Work Order was used for conducting investigations instead of following the established change control procedure. Examples include but are not limited to:

A) There is no procedure to differentiate when events should be documented as a deviation or a work order. Thus, leakage events throughout your facility have been documented as work orders, without a corresponding deviation. Additionally, the work orders have not been the subject of quality oversight and the impact of the event on the facility and associated products have not been performed. Additionally, these work orders have not been trended. For example, the following leaks have been documented as work orders without a corresponding deviation:

Work Order Number	Opened	Description
3296872	January 09, 2025	"Investigation/Actions – A water leak was identified on the (b) (4) (b) (4) On investigation it was found that the (b) (4) was found to not be (b) (4) and was leaking."
3296870	January 09, 2025	"Investigation/Actions – Water was visible on the ground at the (b) (4) (b) (4) On investigation it was found that there were intermittent drops from the (b) (4) (b) (4) and the leak stopped." "Closing Comments - There was no impact on the operation of the system due to this leak and no impact on the operation of the system while repairing leak."
3382891	August 16, 2025	"Water leaking from (b) (4) with no issues noted, (b) (4) closed and inspected from opposite side and no gaps appeared to be present. (b) (4) water leaked from under (b) (4) immediately. (b) (4) stopped to ensure no further water leaked out."

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3384466	August 20, 2025	This work order is associated with work order 3382891 and states (b) (4) leaking" with the investigation identifying (b) (4) liquid was seen coming from (b) (4)
3301730	January 22, 2025	"Action/Investigation – leak coming for (b) (4) leak stopped."
3324758	March 21, 2025	"Investigation/Actions - Water leak on floor underneath (b) (4) identified during (b) (4) on 20 Mar 25. There was initially no sign of the source of the leak in the area at the time. Water was cleaned up and area monitored. On 21 Mar 25 water was again evident in the area. On this occasion water was seen dripping from the (b) (4) (b) (4) and the leak stopped. Residual water was cleaned up and area was monitored with no further issues."

B) Your firm failed to adequately review production records to ensure that no errors have occurred or, if errors have occurred, that they have been fully investigated. There have been (b) (4) failed (b) (4) for (b) (4) (b) (4) since January 2025, attributed by your Area Engineering & Maintenance Manager to improperly (b) (4) No retrospective batch impact assessment has been conducted for these failures, and these recurring events have not been subject to deviation reporting or quality oversight review. Filling Line (b) (4) accounts for approximately 34% of these work orders. Your firm has not conducted retrospective batch impact assessments for these failures, has not subjected these recurring events to deviation reporting or quality oversight review, and has not evaluated whether (b) (4) was compromised during previous batches manufactured using the Grade (b) (4) Line (b) (4) is utilized routinely for filling of U.S. marketed products, including Thymoglobulin and Altuviiio.

C) GMP Permit 240002415 was initiated for Fill Line (b) (4) under Work Order 3350858 to investigate (b) (4) functionality. The investigation was prompted by (b) (4) issues observed during the filling of a previous batch (b) (4) on Fill Line (b) (4) The investigation was conducted under the GMP permit on June 6, 2025. No deviation was initiated for batch (b) (4) in connection with the observed (b) (4) issues.

D) In May 2025, a portion of the (b) (4) in the Grade (b) (4) filling line (b) (4) was identified as a trip hazard. The work order was initiated on January 15, 2026. The GMP permit 260002854 was initiated on January 9, 2026, and approved (by QA) as complete on January 15, 2026. During the inspectional walkthrough on January 13, 2026, we observed that Fill Line (b) (4) was actively being used to fill batch # (b) (4) Thymoglobulin, while this GMP Permit remained open and incomplete. Furthermore, the work order (3447495) was initiated after the FDA made this observation during the inspectional walkthrough.

E) Your (b) (4) electronic quality management system revealed that you cancelled 74 deviations between February 6, 2024, and January 12, 2026. Your cancelled deviations demonstrate a pattern of data entry errors and procedural failures that were not investigated for root cause or addressed through your quality management system. Examples of cancelled deviations include:

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QE-025817 was initiated on April 11, 2025, for Thymoglobulin batch (b) (4) after a team member observed a broken vial on the (b) (4) The deviation was subsequently cancelled based on a QA Expert Comment stating that (b) (4) (b) (4) Fill (b) (4) does not give instruction or advisory for a deviation to be raised in relation to the discovery of a broken vial in the (b) (4) therefore, QE-025817 will be cancelled." The cancellation of this deviation resulted in no evaluation of the potential implications of the broken vial incident. The firm did not assess potential contamination risks to the batch, evaluate the integrity of the sterile environment, determine if other vials in the batch were compromised, implement corrective and preventive actions, or document the incident for future reference. The deviation was closed without investigation of the quality event.

QE-137282 (initiated April 7, 2025): Cancelled after (b) (4) reclassified 13 defects from (b) (4) (b) (4) to "Incorrect Fill Level (b) (4) ". reducing percentage from (b) (4) to (b) (4) below reject limit.

QE-163002 (initiated May 9, 2025): Cancelled as "raised in error" for incorrect defect type entry "foreign matter on body" in EBR defect log.

QE-152679 (initiated July 1, 2025): Cancelled for missing logbook entries based on "presence of a second GMP source".

QE-134066 (initiated March 27, 2025): Cancelled for incorrect (b) (4) confirmed from original GMP source with manufacturing and QA agreement.

QE-094631 (initiated November 17, 2024): Cancelled as "raised in error, no longer required and can be voided" with original deviation description overwritten.

QE-090910 (initiated November 5, 2024): Cancelled as "raised in error and no longer required" for incorrect (b) (4) number logging ((b) (4) vs (b) (4)) with original fields overwritten.

You confirmed that no retrospective impact assessment was conducted for these cancelled deviations. All deviations pertain to U.S. marketed products.

OBSERVATION 3

Buildings used in the manufacturing, processing and holding of a drug product are not maintained in a good state of repair.

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Specifically, the following conditions were observed in your fill/finish manufacturing areas during the current inspection:

A) On January 13, 2026, in Room (b) (4) (Fill Line (b) (4) the (b) (4) exhibited two "X" shaped cracks that were actively extruding water during the (b) (4) operations utilizing (b) (4) The intersecting cracks created four distinct arms, each measuring approximately 4 to 5 inches in length. Your firm's personnel stated they had been aware of these cracks since October 2025, yet continued manufacturing operations without adequate documentation or quality assessment of the water leak's impact on product quality. Despite awareness of (b) (4) cracks since October 2025 and ordering replacement parts in October 2025, there was an absence of GMP documentation regarding the (b) (4) condition until January 12, 2026. No quality documentation addressed the impact of active water leakage from the equipment cracks. Batch (b) (4) Thymoglobulin, was being filled on January 13, 2026, when this observation was made.

B) On January 12-13, 2026, in the Grade (b) (4) area (Room (b) (4)) of Fill Line (b) (4) HEPA filters supplying clean air exhibited reddish brown discoloration consistent with rust. (b) (4) particulate matter consistent with (b) (4) was observed on the Grade (b) (4) floor, and localized areas accumulated significant (b) (4) residue. Batch (b) (4) of Myozyme was being filled when this observation was made.

C) During the inspectional walkthrough on January 13, 2026, we observed a section in the Grade (b) (4) Filling Line (b) (4) (Room (b) (4)) where a portion of the (b) (4) had been removed. The floor in this area exhibited visible discoloration and stains. Multiple holes remained in the floor from the removal of (b) (4) At least one of the holes contained visible blackish-brown liquid of unknown origin. Thymoglobulin batch (b) (4) was being filled in the room while this observation was made.

Note: Fill lines (b) (4) and (b) (4) are routinely used for U.S. marketed drug products, including Thymoglobulin and Altuviiio.

OBSERVATION 4

Equipment and utensils are not cleaned and maintained at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically,

A) On January 12, 2026, filling (b) (4) used for (b) (4) contained unknown brownish white residue around the (b) (4) Internal inspection revealed brownish red discoloration consistent with rust on product contact surfaces, which your firm confirmed as "active corrosion." This (b) (4) was recently used to manufacture

Myozyme batch (b) (4) This (b) (4) is used for routine manufacturing of U.S. marketed products.

B) On January 12, 2026, filling (b) (4) exhibited similar internal product contact surface deterioration with brownish red discoloration and scratches/abrasions to the (b) (4) interior, confirmed by your firm as "scratches and gouges" and "active corrosion." This (b) (4) was recently used to manufacture Thymoglobulin batches (b) (4) and (b) (4) This (b) (4) is used for routine manufacturing of U.S. marketed products.

C) During the filling of Thymoglobulin batch (b) (4) on January 13, 2026, a stopper was discovered on the floor beneath the (b) (4) in Room (b) (4) The stopper was located upstream from (b) (4) filling line. Manufacturing personnel indicated that the stopper could have fallen during (b) (4) operations when the (b) (4) are challenged.

OBSERVATION 5

There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Specifically,

A) Complaint 493112 pertaining to "Foreign Matter After Reconstitution" found in Thymoglobulin lot (b) (4) described brown particulate or blemish on the inside of the vial that was removable when wiped with a cloth. The associated Deviation WATD23E0198 documented that during inspection of Thymoglobulin batch (b) (4) vials were rejected for the (b) (4) defect of foreign matter on stopper, with (b) (4) vials classified as (b) (4) foreign matter. Your firm's engineering investigation concluded that "the most probable root cause of the Foreign Matter observed in PE 100378833 is (b) (4) as a consequence of the (b) (4) manufacturing process." Despite identifying the manufacturing process as the most probable root cause of this critical defect, your firm classified the deviation as (b) (4) and deemed the finding non-reportable. Your firm's justification that removing defective vials negated the impact of the deviation, fails to address the underlying manufacturing process deficiency that generated the foreign matter contamination. Batch (b) (4) was released to the U.S. market (Expired (b) (4)).

B) Deviation WATD23E0838 documented OOS activity results of (b) (4) for batch (b) (4) at the (b) (4) Bioburden (b) (4) stage and an OOS result for PPQ batch (b) (4) at the (b) (4) (b) (4) stage. The firm's investigation concluded that sample contamination with (b) (4) during (b) (4) was the

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probable root cause and determined "no impact to the PPQ program." However, this conclusion was based on a hypothesis of sample contamination with (b) (4) that lacked sufficient evidence.

OBSERVATION 6

Deviations from written production and process control procedures are not justified.

Specifically, Batch (b) (4) of Thymoglobulin was filled under conditions that significantly deviated from qualified operating conditions within the Grade (b) (4) During inspectional walkthrough on January 13, 2026. we observed the (b) (4) and (b) (4) overflowed due to a malfunctioning (b) (4) causing (b) (4) to (b) (4) on the fill line and (b) (4) necessary for maintaining (b) (4) The blocked (b) (4) (b) (4) compromised the (b) (4) ability to maintain the required (b) (4) for Grade (b) (4) environmental classification. No deviation was raised for these non-conforming conditions. and the decision to proceed with batch filling was made under a work order without proper risk assessment of the altered environmental conditions. (b) (4) studies conducted under dynamic conditions demonstrate that these (b) (4) must remain clear of obstructions to maintain (b) (4) (b) (4) during the (b) (4) operation.

*DATES OF INSPECTION

1/12/2026(Mon), 1/13/2026(Tue), 1/14/2026(Wed), 1/15/2026(Thu), 1/16/2026(Fri), 1/19/2026(Mon), and 1/20/2026(Tue).

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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 judgment, 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."