

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

DISTRICT OFFICE ADDRESS AND PHONE NUMBER New England District Office 1 Montvale Ave, Stoneham MA, 02180 781-587-7500 ORAPharm1_responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	DATE(S) OF INSPECTION 7/18/2022 - 7/22/2022, 7/25/2022
	FEI NUMBER 1220423

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Larry Yudiski - Head of 8 New York Avenue Manufacturing and Interim Site Head

FIRM NAME Genzyme Corporation	STREET ADDRESS 68 New York Ave
CITY, STATE AND ZIP CODE Framingham, MA 01701-8861	TYPE OF ESTABLISHMENT INSPECTED 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:

Amendment# 1

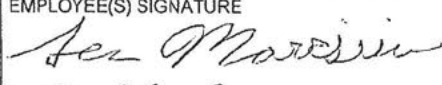

OBSERVATION 1

Failure to exercise sufficient controls over computerized systems and failure to have adequate controls to prevent omission of data.

Specifically,

The firm utilizes (b) (4) testers (b) (4) testers) for (b) (4) testing of cell culture and (b) (4) process (b) (4) during Thyrogen (Thyrotropin alfa) bulk drug substance manufacture. An audit trail review assessment as required per procedure BQ-GOP-000300 "A Risk Based Approach to Audit Trail Review (ATR) for Computerized Systems" – version 3.0, effective date 04/07/2022, has not been performed for the (b) (4) (b) (4) testers utilized for critical GxP decision points during Thyrogen bulk drug substance manufacture. Additionally, no review of the electronic logs/audit trails of the (b) (4) (b) (4) testers was performed to ensure all GxP data are reviewed and incorporated into the firm's manufacturing records and MES logbooks. For example, on 6/9/2022, the firm (b) (4) tested the (b) (4) (b) (4), which was documented as passing specification in the firm's logbook. On 7/19/2022, we reviewed the (b) (4) tester (tester# 3000242) electronic results log and noted (b) (4) additional tests for the (b) (4) which included two failed tests and a canceled test by an operator (as evidenced by code ID: 9175). The two failed and cancelled tests were not recorded in the firm's MES logbook, and no documentation was made as to why the test was cancelled. Since January of 2020, the firm has manufactured (b) (4) lots of Thyrogen bulk drug substance utilizing data from the (b) (4) testers without adequately reviewing the electronic logs/audit trails of the testers.

Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE 	EMPLOYEE(S) NAME AND TITLE (Print or Type) SEAN MARCIS - INVESTIGATOR	DATE ISSUED 7/25/2022
		Daniel Zheng - Investigator	

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

DISTRICT OFFICE ADDRESS AND PHONE NUMBER New England District Office 1 Montvale Ave, Stoneham MA, 02180 781-587-7500 ORAPharm1_responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	DATE(S) OF INSPECTION 7/18/2022 - 7/22/2022, 7/25/2022
	FEI NUMBER 1220423

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Larry Yudiski - Head of 8 New York Avenue Manufacturing and Interim Site Head

FIRM NAME Genzyme Corporation	STREET ADDRESS 68 New York Ave
CITY, STATE AND ZIP CODE Framingham, MA 01701-8861	TYPE OF ESTABLISHMENT INSPECTED Drug Substance Manufacturer

Amendment# 1

OBSERVATION 2

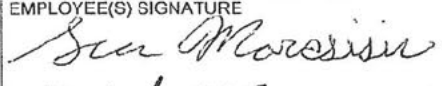

Failure to properly maintain buildings and facilities used in the manufacture of bulk drug substances.

Specifically,

The firm does not properly maintain building 51 which is utilized for Thyrogen bulk drug substance manufacture. During the current inspection, the following items were noted:

- On 7/18/2022, we noted what appeared to be rust on the interior of the sash handle within the grade-A area for biological safety cabinet (BSC# FB-2074 in room 87. The firm was able to wipe and dislodge the material that appeared to be rust within the grade-A area. Room 87 (grade-C room) is the firm's (b) (4) area and is utilized for the (b) (4) manufacturing steps of Thyrogen bulk drug substance. What appeared to be rust was also noted on the exterior of the hood and on ceiling grates in room 87. Thyrogen bulk drug substance lot CGFPS003 was manufactured in room 87 utilizing BSC# FB-2074 in April 2022.
- On 7/18/2022, we noted that the floors within grade-C rooms 152A and 152B were chipped in multiple areas throughout the rooms. Rooms 152A and 152B are utilized for (b) (4) manufacturing activities for Thyrogen bulk drug substance.
- On 7/20/2022, we observed a puddle of unidentified standing liquid in the grade-D room ~~190~~ 140, located underneath and behind the (b) (4), while the room was in use for production of commercial Thyrogen product (lot CGF2B08). We also observed cracks in the floor adjacent to the noted puddle.
- On 7/19/2022, we observed what appeared to be a leak from a (b) (4) for (b) (4) which puddled on the floor in grade-D Room ~~190~~ 140 while the room was in use for production of commercial Thyrogen product.
- On 7/22/2022, we observed what appeared to be a leak from an (b) (4) (#AE-971003) for the firm's (b) (4). The firm's (b) (4) system is utilized for Thyrogen bulk drug substance manufacturing activities and to feed the firm's (b) (4) system in building 51.

Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE  	EMPLOYEE(S) NAME AND TITLE (Print or Type) SEAN MOROSINI - INVESTIGATOR Daniel Zheng - Investigator	DATE ISSUED 7/25/2022
-----------------------------------	---	---	--------------------------