DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
1201 Main Street, Suite 7200 Dallas, TX 75202 (214)253-5200 Fax:(214)253-5314	1/14/2025-1/24/2025* FEI NUMBER 3027507354

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Laura E. Martin, CEO

FIRM NAME	STREET ADDRESS
Turbare Manufacturing	925 Jeanette Dr
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Conway, AR 72032-6651	Outsourcing Facility

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 OBSERVED:

OBSERVATION 1

There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has been already distributed.

Specifically,

A)During media fill lot (b) (4) your firm recovered mold growth from personnel monitoring results of 1 CFU on the right chest sample. This technician was performing compounding activities in the ISO-5 hood for the media fill. Your firm identified the species of mold, *Curvularia intermedia,* but did not perform any investigation to determine where the mold originated or evaluate patient safety due to the presence of this mold on your personnel performing repackaging activities. Your firm's routine environmental monitoring procedure states that "Action responses are always triggered for viable samples regardless of CFU count when CFU identified are of any highly pathogenic organisms such as gram-negative rods, coagulase positive *Staphlyococcus species*, molds, or yeasts.

B)Your firm initiated an investigation into a personnel monitoring result of 1 CFU for fingertip monitoring for lot (b) (4) The result was initially discovered on 11/19/2024. Your firm performed an investigation into this out of specification on 1/14/2025 with no documented justification for the lapse in time for not investigating this critical environmental result. Lot disposition decisions were made prior to the investigation opening. This lot was rejected and destroyed without a documented disposition decision from quality or a record of the destroyed lot.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Logan T Williams, Investigator X Logan T Williams Investigator Signed By: 2002955055 Date Signed: 01-24-2025 10:05:03	1/24/2025

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C)Your firm failed to identify and open investigations for apparent AQL failures for Avastin repackaged lot (b) (4) and (b) (4). These lots were both released and distributed by your firm.

OBSERVATION 2

Acceptance criteria for the sampling and testing conducted by the quality control unit is not adequate to assure that batches of drug products meet appropriate statistical quality control criteria as a condition for their approval and release.

Specifically,

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Your firm's AQL sampling of (b) (4) of the batch (b) (4) syringes) is not statistically significant. In addition, acceptance criteria is not appropriately applied from AQL results.

Avastin repackaged lot (b) (4), expiry 4/18/2025, had two major defects identified, both for particulate matter, during AQL sampling out of (b) (4) syringes evaluated. Your firm's AQL limit for major defects is (b) (4) Your firm calculated the AQL limit against the (b) (4) of (b) (4) syringes resulting in 0.3% major defects. Two syringes out of (b) (4) represents approximately (b) (4) major defects in the AQL sample. Your firm passed this AQL result with no investigation or additional product inspection. This batch was released for distribution.

Avastin repackaged lot (b) (4) expiry 3/14/2025, failed initial 100% visual inspection and was reinspected. After the 200% inspection was complete an AQL was performed. This AQL was performed with a sample size of (b) (4) syringes. One major defect for underfill was found during this AQL. Your firm's AQL limit for major defects is (b) (4). Your firm reported a result against the (b) (4) of (b) (4) syringes and resulting in 0.1% major defects. One out of (b) (4) represents approximately (b) (4) major

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defects in the AQL sample. Your firm passed this AQL with no investigation or additional product inspection. This batch was released for distribution.

OBSERVATION 3

Control procedures are not established which validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product.

Specifically,

The defects contained in the visual inspection qualification kit are not well defined and contain approximately (b) (4) defects. Your firm's classification of defects is not scientifically justified. Your firm's critical, major, and minor defect classifications are not defined in any procedure and defects have not been assessed for risk to patient. According to your firm's CEO, the defects for each category are:

Critical: (b) (4), and (b) (4)

Major: (b) (4) and (b) (4)

Minor: (b) (4)

OBSERVATION 4

Employees engaged in the manufacture and processing of a drug product lack the training and experience required to perform their assigned functions.

Specifically,

1) Qualification of your visual inspectors is deficient, for example:

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- Your firm does not qualify inspection speed. During production (b) (4) syringes can be inspected in less than (b) (4), however, no documented inspection time was recorded during qualification activities.
- The characteristics of the defects within the qualification kit are not well defined. For example, particulate defects are listed as (b) (4)" or "dark" particulate matter of unknown size and composition. Your firm cannot evaluate the capabilities of visual inspectors without developing a well defined qualification kit.
- Your firm does not simulate fatigue during qualification.
- Defects in the qualification kit were prepared in house and the kit does not contain defects based on rejects from actual production. Particulate defects made in house do not necessarily represent defects that would be found from production.

2) Your firm does not have a reject library from which training and familiarization of defects can be studied by new hires or for refresher training.

OBSERVATION 5

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile did not include adequate validation of the aseptic process.

Specifically,

Aseptic processing simulations were performed without protocols developed for defining acceptance criteria and worst-case conditions to be simulated. Your firm is currently performing media fills on the (b) (4) syringe size at (b) (4) of routine batch size without a documented rationale. According to your firm's CEO, this reduced batch size is used after process validation has been completed and operator qualification is being performed.

In addition, your firm qualified operators utilizing various syringe sizes; (b) (4), and (b) (4) without a documented rationale for this bracketing. Your firm's current commercial product uses a

(b) (4) syringe size with a batch size of (b) (4) syringes. The (b) (4) syringe media fill is approximately (b) (4) syringes with a shorter fill time and different processing steps than commercial production.

OBSERVATION 6

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established and written.

Specifically,

Your firm's media fill procedure, SOP-039, was not implemented prior to performing media fills. Your firm's media fill procedure was implemented on 6/12/2024. This procedure does not define acceptance criteria, routine and non-routine interventions to be performed, fill volume, or minimum fill time to be achieved for each process to be simulated.

Your firm performed (b) (4) media fills prior to implementing any media fill procedure. In addition, no media fill protocols were developed until 11/21/2024. Interventions performed were not documented until protocols were developed. One technician used in routine production has not performed a media fill on the 0.25mL syringe process since procedures were developed.

OBSERVATION 7

Your firm failed to establish written procedures for production and process controls designed to assure that the drug products have the identity, strength, purity, and quality that they are purported or represented to possess.

Specifically,

Your firm does not have a procedure to govern environmental monitoring investigations into alert and action limits being reached during routine sampling. Your firm's investigation procedure, Investigation

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Program, SOP-081, effective 1/7/2025, states that the routine environmental monitoring procedure governs excursions and investigations in environmental monitoring. The routine environmental monitoring procedure does not require an investigation into action levels being reached for sample results. Action responses are not defined within the environmental monitoring procedure.

OBSERVATION 8

Laboratory records do not include the initials or signature of a second person showing that the original records have been reviewed for accuracy, completeness and compliance with established standards.

Specifically,

Your firm does not require a second reviewer for environmental monitoring results unless (b) (4) colony forming unit (CFU) is found. A single technician reads environmental plate counts and the worksheet with results is later reviewed, however, the physical plates are not verified unless growth is present.

*DATES OF INSPECTION

1/14/2025(Tue), 1/15/2025(Wed), 1/16/2025(Thu), 1/17/2025(Fri), 1/21/2025(Tue), 1/22/2025(Wed), 1/24/2025(Fri)

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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."