DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
CDER/OPQ/OPMA/DPMA VI 10903 New Hampshire Avenue; White Oak Building 51/Room 2269 Silver Spring, MD 20993-0002 E-mail: OPMABLAInspection483Responses@fda.hhs.gov	08/20/2024-08/23/2024; 08/26/2024-08/28/2024; 08/30/2024 FEI NUMBER 2246315

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Leticia Fabiano, Vice President / Ridgefield Site Head

FIRM NAME	STREET ADDRESS
Genzyme Corporation	1125 Pleasant View Terr
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Ridgefield, NJ 07657-2310	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

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,

A. Your program for the visual inspection of sterile injectable drug products does not provide adequate assurance that finished products manufactured at your facility possess their purported quality attributes, including that they are essentially free from particulate matter. This is evidenced by:

   i. Your firm failed to adequately validate your (b) (4) visual inspection (b) (4) process for (b) (4) Specifically,

      a. No evidence was provided that, during (b) (4) qualification runs (SAT, IQ, OQ), the correct rejection (b) (4) rejection priority (*i.e.*, rejection of units with several defects (b) (4) and counting of rejects were adequately verified.

      b. The (b) (4) qualification (b) (4) study) for (b) (4) is deficient. For example,

         - The (b) (4) sets used for (b) (4) were created based on the (b) (4) study outcomes. No process risk assessment was performed for (b) (4) or (b) (4) to identify the types of particulate, or other visual inspection defects, that could be potentially present in the product and therefore should be included in the (b) (4) sets.
         - The (b) (4) sets used for (b) (4) did not include particulate and fiber defects at the detection level threshold, *i.e.*, (b) (4) µm (all types of particles in (b) (4) mL set and (b) (4) particles in (b) (4) mL set) and ~ (b) (4) µm (white fiber, both (b) (4) mL and (b) (4) mL sets), respectively.
         - The (b) (4) visual inspection (b) (4) threshold limits established during the (b) (4) studies for (b) (4) mL fill volume, show that your firm's inspectors can

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detect particulates within the range of (b) (4) µm with a probability of detection (PoD) of (b) (4) % and fibers within range of (b) (4) µm with a PoD of (b) (4) %. Similarly, for (b) (4) mL fill volume, your firm's inspectors can detect particulates within the range of (b) (4) µm with a PoD of (b) (4) % and fibers within range of (b) (4) (b) (4) µm with a PoD of (b) (4) %. The outcomes of the studies do not support that your (b) (4) process can adequately detect particulate ranges of (b) (4) µm (b) (4) µm for fibers) with a PoD of (b) (4) % or greater.

- (b) (4) validation runs during (b) (4) studies did not adequately challenge the equipment/process to ensure the (b) (4) can correctly identify defective units interspersed within the good units during the production runs and reject them (b) (4) (b) (4) Specifically, all good units of the (b) (4) set and units with cosmetic and particulate defects were run separately, (b) (4) (b) (4) Defective units were recirculated and not rejected during such runs.

c. The (b) (4) PQ was limited to [redacted] filled (b) (4) per run. Although (b) (4) were being validated, for (b) (4) mL fill volumes, a total of (b) (4) runs, (b) (4) (b) (4) filled (b) (4) were performed. No additional (b) (4) PPQ with sample size exceeding production AQL sampling was performed on (b) (4) PPQ lots.

d. (b) (4) reject characterization is limited to [redacted] units (b) (4) This number was exceeded for (b) (4) out of (b) (4) accepted lots (b) (4) reaching (b)(4) in (b) (4) As (b) (4) are setup to prioritize rejection of cosmetic defects over particulates, units with (b) (4) defects will be rejected (b) (4) (b) (4) Similarly, rejection of "incomplete inspection" units is prioritized over particulates as well. None of these rejects are subsequently characterized and/or evaluated for presence of particles, including extrinsic particulates.

e. Your firm does not have procedures for identification, trending, and investigation of all extrinsic particle defects. Investigation is opened only in case of a particle limit exceedance.

f. You did not adequately define reject limits for critical, major, and minor defects. Instead, limits were setup for particulate, fill level, (b) (4) (b) (4) defects based on the PPQ outcomes, at (b) (4) %, which exceeded the acceptable limit for critical defects. Some of these categories of rejects include both critical and minor defects. For example, "(b) (4)" reject with established reject limit of NMT (b) (4) % includes both scratches (minor defect) and cracks (critical defect).

g. Your firm lacks an adequate procedure to ensure (b) (4) equipment performance. Specifically,

- There is no requirement for routine requalification of (b) (4) equipment.
- The challenge sets used for verification of (b) (4) performance at the beginning and end of batch and after certain interventions do not include small size defects (both particles and cracks/scratches) to ensure the absence of equipment sensitivity deterioration. For example, scratch defects are (b) (4) mm, particle defects are ~ (b) (4) µm, and fibers are ~ (b) (4) µm.

  Additionally, the challenge sets do not contain several defects included in the (b) (4) sets during (b) (4) validation, for example, overfill (b) (4) mL set), (b) (4) mL set), black mark inside (b) (4) mL sets), embedded foreign matter (b) (4) (b) (4) mL sets), inverted or wrong stopper (b) (4) mL sets).
- You do not perform challenge set runs after extended periods of inactivity during (b) (4) of a batch, for example, after pausing the visual inspection of a batch (b) (4)

h. The (b) (4) are setup to detect (b) (4) between (b) (4) in (b) (4) out of (b) (4) only.

ii. Training and qualification of operators performing visual inspection of (b) (4) are inadequate. Specifically,

a. Both (b) (4) training and qualification sets do not include units with (b) (4) defects, and particulate and fiber defects at the detection level threshold, *i.e.*, (b) (4) µm and ~ (b) (4) µm, respectively. Furthermore, there are no specific qualification requirements for the (b) (4) (b) (4) stopper position detection using (b) (4) Your CAPA 022916 to implement such qualification was opened on 08/16/2024 and is still in progress at the time of the inspection. Training of operators on use of stopper position and (b) (4) is limited to review of MBR (b) (4) and (b) (4) hands-on demonstration.

b. Your SOP-0006963 "Training, Certification and Recertification of Visual Inspectors and Characterizers" (Ver. 16.0, effective 08/02/2024) does not require (b) (4) consecutive passing tests for qualification. According to the SOP, up to (b) (4) attempts at each test are allowed.

iii. Your Acceptable Quality Limit (AQL) sampling and testing process is deficient. Specifically,

a. AQL samples are not representative of the final batch as they are not taken from the units

accepted by the (b) (4) Instead, (b) (4) are sampled during a filling run and are visually inspected before the rest of the batch. Units accepted by (b) (4)

b. The criticality classification of AQL visual inspection defects does not always commensurate with their potential sterility and therefore patient safety impact. For example, product in (b) (4) is considered minor or acceptable defect unless (b) (4) is observed. Similarly, embedded foreign matter on stopper (b) (4) is considered a minor defect.

B. Your firm have not established adequate process controls for commercial (b) (4) (b) (4) mL fill volumes). This is evidenced by the following:

i. You have not qualified the inspection procedures to (b) (4) inside the (b) (4) during the aseptic filling/stoppering in-process check, and the AQL sampling and testing at batch release. Appropriate threshold (sensitivity) studies have not been conducted to demonstrate your firm's visual inspection process capability to remove the (b) (4) (b) (4) greater than (b) (4) (a critical defect) from the (b) (4) drug product (DP) manufactured at your facility.

ii. You have not provided adequate scientific justification for the sampling frequency (approximately (b) (4)%) for the (b) (4) in-process monitoring during the (b) (4) DP aseptic filling/stoppering operation. The in-process sampling plan for (b) (4), with no (b) (4)% (b) (4) (b) (4) testing at batch release, does not result in statistical confidence in your process performance to demonstrate that the batch is essentially free of the critical "(b) (4)" defects.

iii. You failed to ensure that the critical process parameter of (b) (4) is not exceeded during the batch production. The instrumentation used for the (b) (4) monitoring does not continuously record (b) (4) Nor is the (b) (4) alarmed. The operators only record the (b) (4) exceeding normal operating range of (b) (4) observed during manufacture of lot (b) (4) was investigated under QE-051072. No CAPAs were proposed for implementation of either (b) (4) alarm (b) (4) monitoring at the conclusion of the investigation. The deviation was closed on 06/28/2024.

OBSERVATION 2

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

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Specifically,

A. While observing the aseptic setup operations on the (b) (4) Filling Line for the filling of (b) (4) (b) (4) DP (Lot # (b) (4) on 26 August 2024, the following deficiencies were noted:

i. While installing the (b) (4) stoppering system, the operator touched the indirect product-contact sterile parts with the non-sterile (b) (4) In addition, the operator placed a non-sterile tool (wrench) on the exposed stopper track.

ii. While installing the filling assembly, the operator blocked the first air over the exposed (b) (4) (b) (4) stoppering parts with non-sterile (b) (4) In addition, the operator was observed resting his right arm by placing the (b) (4) on the top of the stoppering station.

iii. While removing the waste materials from inside the RABS, the operator passed the non-sterile wrapping materials over the exposed (b) (4) stoppering parts and stopper track to the operator located on the other side of the RABS for disposal.

iv. While removing the (b) (4) wraps from stopper system (b) (4) (b) (4) the operators blocked first air over the exposed sterile surfaces of these indirect product-contact equipment with the non-sterile exterior surface of (b) (4) wraps.

B. While reviewing the dynamic smoke study videos (QU-OPE-1924404 and VRMM0198-1-1) for the (b) (4) Filling Line, the following deficiencies were noted:

i. Your firm failed to perform adequate smoke studies to demonstrate unidirectional airflow and sweeping action over and away from sterile equipment surfaces, and container/closure systems in your aseptic operations. Specifically, the documented smoke studies do not reflect actual operations since they lacked simulation of multiple critical interventions that occur during aseptic manufacturing operations for (b) (4) DP. For example,

a. The aseptic set-up process was excluded from the studies;

b. The following corrective interventions were excluded from the studies:
- Changing (b) (4)
- Clearing jammed stopper at (b) (4) and,
- Adjustment of (b) (4)

ii. Poor aseptic practices captured in the smoke study videos were not identified and addressed

during the final quality review and approval of the studies. In particular, while installing the (b) (4), the operator was observed placing non-sterile (b) (4) over the exposed direct product-contact surfaces of (b) (4). In addition, operators were observed touching the unprotected (b) (4) of the (b) (4) with the (b) (4) while attempting to connect the (b) (4) tubing to the (b) (4) (b) (4)

iii. Documentation of the airflow pattern visualizations is deficient in that the videos do not afford an ability to visually observe the unidirectional airflow and/or the air turbulence that may be caused by the interventions. Specifically, airflow patterns were not visible and could not be evaluated due to insufficient smoke, obstructions, and poor camera angles.

C. Environmental monitoring (EM) of aseptic processing areas were found deficient. For example,

i. During the routine EM following the filling activities, no microbiological surface samples were taken from stopper-contact surfaces of the (b) (4) stoppering system (*e.g.*, (b) (4) (b) (4) or from the stopper-contact surfaces of stopper track, (b) (4) (b) (4) and stopper chutes. In addition, microbiological surface samples were only taken from (b) (4) of (b) (4)

ii. During the routine EM following the aseptic set-up activities, personnel contact-plate samples were not taken from the primary operators' foreheads. The operators placed their heads and upper torsos inside of the Grade A RABS to perform the set-up activities. In addition, the goggles used by the operators have gaps on the sides of the goggles.

iii. Your firm's EM program does not include appropriate measures to monitor, trend and control fungal (mold) and spore-forming bacteria contamination in the grade C and D manufacturing areas. Specifically, appropriate alert or action limits have not been established for mold and spore contamination in these classified areas. Only a cumulative account of bacterial and fungal colonies is evaluated against the alert/action limits. Consequently, the EM program lacks assurance of a timely and sensitive detection of adverse trend of mold or spore contamination in your sterile DP manufacturing facility.

D. Your firm lacks an established cleaning and sanitization program to prevent the introduction of microbial contamination into controlled sterile DP manufacturing environments. In particular,

i. Your disinfectant surface-challenge study (RMB0185-0-2, Revision 1.0) was performed by applying sanitizers to be validated onto (b) (4) surfaces, then cleaning surfaces using sterile wipes and sterile mop heads prior to surface sampling. Consequently, the study failed to

determine the effectiveness of the sanitizers used in your facility.

ii. Your disinfectant efficacy study does not adequately support the sanitization procedures for the antimicrobial and sporicidal effectiveness of the disinfectant and sporicidal agent for all representative manufacturing surfaces in your facility. For example, materials used for (b) (4) (b) (4) were excluded from the study. In addition, the study failed to include the (b) (4) sanitizer(s) used in the aseptic operations.

iii. The non-product contact surfaces within the (b) (4) Filling Line RABS are not disinfected with a suitable sporicidal agent prior to each sterile DP manufacturing campaign. Per QU-SOP-0011583 (version 31.0), the sporicidal agent, (b) (4), is only used for the RABS disinfection (b) (4)

E. Qualification of aseptic personnel does not require performing all critical interventions during aseptic process simulation (media fill, MF). Specifically, (b) (4) aseptic operators were certified for Grade A and B interventions through (b) (4) media fill runs: (b) (4) No evaluation was conducted to ensure that each of the certified operators had performed all routine and corrective critical interventions, including the complete aseptic set-up processes of filling and (b) (4) stoppering parts, during these MFs.

OBSERVATION 3

Written records of investigations into unexplained discrepancies, the failure of a batch or any of its components to meet specifications, do not always include appropriate documentation, conclusions, and follow-up.

Specifically,

A. Deviation QU-022745 was initiated for a validation failure during the (b) (4) process performance qualification (PPQ). The first PPQ run (PPQ1, Lot (b) (4) was aborted due to product observed in (b) (4) stoppers, and in the (b) (4) Your firm's investigation attributed the root cause of the PPQ failure to the inappropriate (b) (4) surrogate (*i.e.*, (b) (4) utilized for optimization of (b) (4) stoppering settings during the "engineering" run. A limited experiment performed by the vendor technician during troubleshooting to adjust the settings was not sufficiently documented. With the adjusted (b) (4) settings, your firm then proceeded to complete the (b) (4) PPQ runs and subsequently manufactured (b) (4) commercial (b) (4) lots. Process design studies following sound scientific methods and principles were not conducted prior to recommencing the PPQ runs. In addition, your deviation investigation failed to

identify that the (b) (4) of (b) (4) filler had a (b) (4) deviation from calibration standards, which can have a significant adverse impact on the expected operating ranges of (b) (4) mL fill volumes, respectively). Consequently, there is lack of assurance that the critical process parameters for the (b) (4) stoppering are suitable for routine commercial manufacturing that can consistently deliver a product that meets its safety and quality attributes.

B. Deviation QE-040663 was initiated for acceptance of (b) (4) with fill weight outside of specification. The investigation attributed root cause of the deviation to lack of procedures for evaluation of (b) (4) reports showing accept/reject status for (b) (4) rejected by the filler. Additionally, multiple (b) (4) rejected by the filler after start of filling but prior to initiation of IPC by filling operators ("no IPC" alarm) or due to other code (b) (4) alarms were accepted by operators due to misinterpretation of (b) (4) reports. Your investigation established that the impact across batches (b) (4) (b) (4) was limited to (b) (4) incorrectly accepted (b) (4) The investigation concluded that there was no impact to validation or product and all batches were acceptable for release. The deviation was closed on 07/12/2024.

The following issues not identified during your batch review or considered during the deviation investigation, corrective actions, or product and validation risk assessment were noted during review of the deviation investigation and associated documentation:

- A total of (b) (4) (up to (b) (4) processed prior to IPC function initiation in lots (b) (4) do not have associated (b) (4) reports. No documentation of these (b) (4) rejection was provided.
- There were multiple instances of operators turning IPC function on and off after initiation of fill of batches (b) (4)
- Numerous unexplained discrepancies between (b) (4) reports and filler batch reports with respect to (b) (4) IPC status, rejection status, etc. were noted.

  For example, for lot (b) (4)

  IPC was initiated starting from (b) (4) but only (b) (4) was rejected according to the (b) (4) reports. (b) (4) etc. were subjected to IPC with acceptable result but were still rejected with "no IPC" alarm. According to the (b) (4) reports, these (b) (4) were not considered IPC (b) (4) by the filler despite being sampled per the (b) (4)

(b) (4) were not subject to IPC (b) (4) but were rejected with "no IPC" alarm.

According to the (b) (4) reports there was an IPC change between (b) (4) filled at (b) (4) and (b) (4) filled at (b) (4) on 04/08/24. No IPC frequency changes were made during this timeframe per the audit trail in the batch report.

For batch (b) (4) the following was noted:
(b) (4) were not subject to IPC (b) (4) but were rejected as out of weight limit.

- Multiple instances of incorrect IPC sampling and/or rejection by the filler. For example,

Although (b) (4) should be sampled in batch (b) (4) (b) (4) were sampled, at which point the filler continued IPC of (b) (4) (b) (4) was sampled, and so on. You explained that skipped (b) (4) were "(b) (4)", i.e., rejected by operators. However, no records of such rejections were provided.

During (b) (4) IPC sampling performed for all (b) (4) of the (b) (4) of lot (b) (4) (b) (4) contained over the action limit (b) (4) contained over alert limit units. According to the (b) (4) report, (b) (4) were not rejected. The (b) (4) did not continue (b) (4) IPC until (b) (4) of within alert limit units were obtained and instead proceeded with intermittent IPC of (b) (4) (b) (4)

According to the batch report for lot (b) (4) IPC was performed on (b) (4) (b) (4) used for (b) (4) contain (b) (4) Over action limit units were in (b) (4) (b) (4) However, (b) (4) were not marked as rejected in the corresponding (b) (4) report.

C. Deviation investigation and associated CAPAs do not always extend to other potentially impacted batches, products, and/or processes. For example,

You initiated QE-033408 and QE-035325 for exceedances of (b) (4) and particle defects, respectively during (b) (4) of (b) (4) lots (b) (4) Root cause was identified as (b) (4) due to variability of (b) (4), where (b) (4) is (b) (4) of the (b) (4) Resulting false rejection of (b) (4) were remediated via changes in the inspection (b) (4) location for (b) (4) mL (b) (4) per (b) (4) You failed to assess if a similar update to (b) (4) mL (b) (4) was needed.

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Deviation QE-043392 was opened for an AQL inspection failure for (b) (4) lot (b) (4), which shares (b) (4) equipment with (b) (4) The root cause was determined to be a low (b) (4) detection threshold resulting in false detection of (b) (4) in empty (b) (4) The (b) (4) was updated to adjust threshold settings per (b) (4) The deviation was closed on 07/21/2024 without an evaluation for potential need for implementation of similar changes in the (b) (4) for other products, including (b) (4)

D. Deviation QE-035410 was initiated for (b) (4) count mismatch between batch report (b) (4) accepted) and (b) (4) identified during manufacture of (b) (4) lot (b) (4) The investigation included (b) (4) count of (b) (4) rejects, that discovered a mismatch between (b) (4) count (b) (4) of cosmetic rejects. Following the counter functional test, which did not identify a malfunction, you attributed the root cause of good (b) (4) count mismatch to poor segregation of inspected and uninspected (b) (4) No further investigation into mismatch of the defect counts was performed and no CAPA was proposed for implementation of (b) (4) reconciliation of rejects. The deviation was closed on 06/21/2024.

E. Deviation QE-015182 was initiated for an action level recovery in Grade B: (b) (4) cfu of mold *Chaetomium cruentum/globosum*, which is associated with water-damaged buildings. The mold was recovered on the (b) (4) surface of (b) (4) tank (b) (4) which was stored in an CNC area and cleaned (b) (4) prior to entry into Grade B area. Your root cause investigation failed to identify potential sources of the contaminant and failed to assess the effectiveness of your equipment cleaning and disinfection procedures. The deviation was closed on 04/03/2024.

F. Deviation QE-033078 was initiated for incorrect lot number printed on shipper labels for (b) (4) lot (b) (4) Human error was identified as the root cause of the deviation. Specifically, you determined that operators did not ensure that previous batch data was removed from the associated computer systems prior to initiation of packaging of lot (b) (4) and did not perform label information verification during any of the (b) (4) in-process checks. Despite this, all the steps were initialed and signed by the performer and verifier (previous batch data removal step only). Contributing factors were similarity in the previous and current batch numbers, lack of procedure understanding, absence of one of Lead Operators (b) (4) and multitasking/overwhelm of the operator. Your CAPAs are limited to an MBR update of adding a batch data removal step at the end of batch, and brief training of packaging operators in human error prevention and ALCOA principles. No actions were proposed to address any of the contributing factors identified or to revise relevant processes to reduce or eliminate opportunities for non-adherence to ALCOA principles and to ensure human error prevention. The deviation was closed on 06/05/2024.

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OBSERVATION 4

Your Quality Unit (QU) is not fully exercising its authority and/or responsibilities to provide adequate oversight throughout your GMP manufacturing operations.

Specifically,

A. Your firm failed to exercise appropriate controls to protect the electronic data acquisition and manufacturing control systems used for the manufacture of (b) (4) drug product. Specifically,

   i. Login identifications unique to each user have not been established for computerized systems. Your staff used the shared username and password to log into the laptops to access the (b) (4) (b) (4) data acquisition systems (IDs (b) (4) for (b) (4) (b) (4) validation of critical process equipment, including (b) (4) validation.

   ii. There is inadequate segregation of duties in the management of user privileges. Specifically, the system administrators for (b) (4) systems (IDs (b) (4) are designated to the staff of the firm's validation group, which is responsible for the validation of the process equipment. The "Administrator" user for the software has unrestricted system and software privileges that allow for the move and deletion of raw data sets and reports.

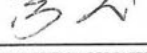
   iii. Your firm's audit trail review process is deficient. For example,

      a. Audit trails enabled in the (b) (4) data acquisition systems are not reviewed for each data set during the equipment (b) (4) validation review process.

      b. Audit trails enabled in the (b) (4) used to control and collect inspection data from the (b) (4) are not reviewed for each data set during the batch record review process.

   iv. Process equipment (b) (4) validation data collected and stored in the (b) (4) (b) (4) data acquisition systems have not been backed up.

B. During (b) (4) troubleshooting of exceedance of (b) (4) defect limits during production of commercial batch (b) (4), User (b) (6) changed the (b) (4) from validated (b) (4) to (b) (4) This change was not documented in the batch record, QU was not informed, and no deviation was opened. The incident was uncovered during investigation of QE-035410. CAPAs specific to this event were limited to CAPA-015516, "a discussion not to change the validated (b) (4) during production batch" with operators, mechanics, and supervisors. No evaluation of QU oversight, permissions in the (b) (4) system, etc. were performed.

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CDER/OPQ/OPMA/DPMA VI 10903 New Hampshire Avenue; White Oak Building 51/Room 2269 Silver Spring, MD 20993-0002 E-mail: OPMABLAInspection483Responses@fda.hhs.gov	08/20/2024-08/23/2024; 08/26/2024-08/28/2024; 08/30/2024
	FEI NUMBER 2246315

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Leticia Fabiano, Vice President / Ridgefield Site Head	
FIRM NAME Genzyme Corporation	STREET ADDRESS 1125 Pleasant View Terr
CITY, STATE, ZIP CODE, COUNTRY Ridgefield, NJ 07657-2310	TYPE ESTABLISHMENT INSPECTED Drug Product Manufacturer

C. Your firm lacks adequate assurance that the critical process equipment, used for the manufacture of (b) (4) DP, is maintained in a validated state. Specifically,

i. (b) (4) (asset ID (b) (4) used in sterilization of (b) (4), fails to have a validation and routine revalidation for the (b) (4) sterilization, physical and biological assessment.

ii. Your firm lacks a preventive maintenance procedure for proper replacement of (b) (4) in the (b) (4) of the (b) (4) filling line.

D. Your quality unit does not fully exercise its responsibilities regarding the critical service contractor qualification. For example, your firm has not conducted any on-site GMP audit of (b) (4) who is responsible for the validation of clean rooms at your sterile DP manufacturing facility.

30 Aug 2024

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE *(Print or Type)*	DATE ISSUED
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