DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
CBER/OCBQ/Division of Manufacturing and Product Quality 10903 New Hampshire Avenue Silver Spring, MD 20993 Lead Inspector: Xiuju Lu TEL: 301-796-2161 Industry Information: www.fda.gov/oc/industry	06/02/2025-06/06/2025 FEI NUMBER 3001451441

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED	
Christophe Royer, Vice President, Site Head	
TO: FIRM NAME Lonza Portsmouth, Inc.	STREET ADDRESS 101 International Drive
CITY, STATE, ZIP CODE, COUNTRY Portsmouth, NH 03801 USA	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

Aseptic processing of CASGEVY drug product is deficient. Through review of closed-circuit television (CCTV) footage on June 04, 2025, during the processing for batch (b) (4), (b) (6), (b) (7)(C) on May 26, 2025, the following was observed:

a. Throughout aseptic processing, Grade (b) (4) operators routinely change sterile (b) (4) in the Grade (b) (4) area where manufacturing is conducted. It was observed that an operator, on multiple occasions, proceeded to perform manufacturing activities following (b) (4) changes without (b) (4) of the (b) (4) Per procedure USPO-15643 titled "Gowning and Personnel Movement for Cell Therapy," (b) (4) changes should be conducted in the (b) (4) Similarly, operators routinely adjusted (b) (4) including the (b) (4) in direct proximity to open manufacturing activities, as opposed to utilizing the (b) (4) as mandated by the aforementioned procedure.

b. Throughout aseptic processing, a Grade (b) (4) operator on multiple occasions reached into the Grade (b) (4) biological safety cabinet (BSC) without taking special precautions (b) (4) as prescribed by procedure USPO-16621 titled "Operation of the Biosafety Cabinet in Cell Therapy" to prevent contamination.

c. Throughout aseptic processing, multiple Grade (b) (4) operators rested/leaned their upper body against a (b) (4) an aseptic operation. The person on a (b) (4) can be seen rolling in a circular motion throughout a portion of the Grade (b) (4) room flanking the BSC where aseptic processing occurs. No (b) (4) occurred prior to returning to manufacturing operations.

d. Your firm's BSC operators (b) (4) (without any subsequent manufacturing activities) immediately prior to performing (b) (4)

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OBSERVATION 2

Cleaning of Grade (b)(4) areas used in the manufacture of CASGEVY drug product is deficient. For example, during an evaluation of cleaning conducted on (b) (4) of rooms (b) (4) respectively, the following deficiencies were noted:

a. During (b) (4) cleaning operations, a cleaning operator retrieved an item from the Grade (b)(4) floor with their (b) (4) hands, and proceeded to operation without (b) (4) as prescribed in procedure USPO-15643 titled "Gowning and Personnel Movement for Cell Therapy".
b. (b) (4) and BSC were largely omitted as a part of cleaning. These areas appeared to be inaccessible to cleaning staff.
c. Cleaning throughout the rooms failed to apply (b) (4) as described in the corresponding work instruction USPO-16065 titled "Cleaning of Grade (b)(4)
d. During the cleaning of Room (b) (4) a dirty mop was left on a multi-use cart, and subsequently removed without disinfecting the multi-use cart.
e. Cleaning activities are (b) (4) without verification of cleaning activities by your firm.

OBSERVATION 3

The following practices that are inconsistent with Good Documentation Practices were observed:

a. Your firm uses (b) (4) to instruct quality control analysts to review/ revise environmental monitoring records. On June 05, 2025, (b) (4) encompassing review comments were observed on a laboratory record and in the trash can to the (b) (4) (Room (b) (4). For example, one (b) (4) reads (b) (4)
b. Five original (b) (4) were identified in the aforementioned trash.
c. The authenticity of documents cannot be established. Specifically, the comment on page 48 of (b)(4), (b)(6), (b)(7)(C) (b)(4), (b)(6), (b) of batch records for lot (b)(4), (b)(6), (b)(7)(C) indicates that spreadsheet was reprinted for clarity on December 18, 2024. The performer's signature dated October 4, 2024, for Step 10.3 was crossed out and replaced with the reviewer's signature dated December 18, 2024. The original excel spreadsheet was not attached to the batch records and remains missing.

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d. Your firm failed to establish documentation, validation, and control of spreadsheets utilized for tracking of (b) (4) For example, uncontrolled spreadsheets is used to track the (b) (4) Separate uncontrolled spreadsheet is used by SOP USP-6090 "Handling and Tracking of Returned Materials for Further Investigation" to (b) (4) There is no defined user accountability, nor adequate controls to prevent uncontrolled modifications to the spreadsheets.

OBSERVATION 4

Heating, ventilation, and air conditioning maintenance and controls are inadequate. For example:

a. There have been repeated losses in differential pressure within the Grade (b) (4) areas for extended periods of time (e.g., July 11, 2024, August 19, 2024, October 08, 2024, October 14, 2024). These events were not deemed deviations, and no root cause or corrective and preventive actions (CAPA) were identified. The pressure differentials within the Grade (b) (4) areas are completely lost. Upon retrospective evaluation in response to FDA request, your firm tabulated that a repeated (b) (4) of the respective fan unit led to the loss of pressure differentials. Nevertheless, you failed to holistically identify or rectify the cause of the (b) (4)

b. Grade (b) (4) areas to Cell Therapy contain HEPA air supply vents adjacent to (b) (4) which lack installation of a (b) (4)

OBSERVATION 5

Areas designed to (b) (4) in a biological safety cabinet are deficient regarding characterization and mapping of the areas and operations for aseptic processing of drug products. Specifically,

a. Turbulent upward airflow was observed in Grade (b) (4) rooms when operators opened (b) (4) in (b) (4)

b. During operations in the BSC, turbulent airflow was observed in the prevailing Grade (b) (4) environment near the operator's (b) (4)

c. Worst-case operations were not challenged during the full dynamic smoke study supporting operations in the BSC, including maximum number of (b) (4) (b) (4)

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d. During the processing for batch (b) (4), (b) (6), (b) (7)(C) (b) (4) on May 26, 2025, a waste bucket was introduced into the BSC (b) (4) in a manner that does not appear slow or deliberate. Your firm failed to emulate similar operations as a part of your dynamic smoke studies.

OBSERVATION 6

Management of deviations and anomalous events is inadequate to identify root causes and appropriate corrective actions. For example:

a. Deviations are cancelled without documented justification. Furthermore, upon cancellation of deviations, your firm deletes the associated deviation information and context from the applicable electronic system, (b) (4) For example, On June 3, 2025, your firm failed to provide adequate reasoning for cancellation of the following deviations:

Deviation	Description	Reasoning for cancellation as provided during inspection
1260276	(b) (4) – Missed witness signature at step 5.7 of (b) (4), (b) (6), (b) (7)(C) for lot (b) (4), (b) (6), (b) (7)(C)	Missing signature can be addressed as a comment in the (b) (4)
1297910	Two (b) (4) workflows (b) (4) (b) (4) had the same (b) (4) printout attachment. Manufacturing team could not locate the correct printout.	Manufacturing team later located the correct printout.
1348179	(b) (4) did not have zero count verification prior to site sampling	(b) (4) counts were successfully performed
1338142	(b) (4) (b) (4) The operator removed (b) (4) when exiting from Grade (b) (4) to Grade (b) (4)	Operator immediately left Grade (b) (4) area. Closed per alignment with (b) (4), (b) (6), (b) (5), (b) (4), (b) (6), (b) (7)(C) and (b) (4)
1328448	Room (b) (4) out emergency release pulled allowing opening (b) (4) doors at (b) (4)	Pulling an emergency lever is not a deviation per (b) (4)

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b. The repeated deviations are not escalated and adequately investigated to prevent re-occurrence. For example:
   i. Three similar repeated deviations were initiated in three consecutive (b) (4) (b) (4) for CASGEVY drug product related to the presence of (b) (4) (b) (4) were identified in 50% of the vials in the three runs (b) (4) The deviations were not escalated, and no further investigation was conducted to implement appropriate CAPAs.
   ii. There have been repeated deviations for personnel who exceed the (b) (4) for remaining in the Grade (b) (4) area before (b) (4) is required, as established in USPO-15643 titled "Gowning and Personnel Movement for Cell Therapy." These deviations were documented in records 1254029 (opened October 03, 2024), 1255104 (opened October 07, 2024), 1262110 (opened October 22, 2024), and 1354895 (opened May 22, 2025). However, despite recurrence of these deviations, the deviation classification was not escalated, and an applicable CAPA has not been identified or implemented.

c. You fail to open deviations in response to non-conforming events documented as comments on your production batch records. For example:
   i. During execution of (b) (4)
      1) (b) (4)
      2)
      3)
      4)
      5)
      6)
   ii. (b) (4) (b) (4) batch (b) (4), (b) (6), (b) (7)(C)

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iii. (b) (4) appeared to have a puncture in one of the (b) (4) and had to be replaced on (b) (4), (b) (6), (b) (7)(C) for batch (b) (4), (b) (6), (b) (7)(C)

OBSERVATION 7

Environmental monitoring and control are deficient. For example:

a. The non-viable particulate monitoring on (b) (4) exceeded the prospective allowable limits. Nonetheless, your firm deemed the results in specification. The determination that the results were in specification was based on an assignment of an (b) (4) status despite no ongoing manufacturing operations.

b. Procedure USPO-1637 titled "Remedial Action for Environmental, Water, Clean Steam, and Gas Monitoring Data" stipulates (b) (4)

(b) (4)

(b) (4) Thus, your response to (b) (4) does not include the appropriate scrutiny and follow-up to address the potential problem.

OBSERVATION 8

Your firm routinely downgrades Grade (b) (4) suites intended for commercial CASGEVY manufacturing (b) (4) (b) (4) to Grade (b) (4) environmental status for the purposes of personnel training. The procedures followed to restore Grade (b) (4) status are inadequate to ensure purported safety of products manufactured in (b) (4) and (b) (4) The following deficiencies were observed:

a. USPO-5217 indicates that (b) (4)
However, the limits applied to the EM data collected, were set at Grade (b) (4) limits, as opposed to (b) (4) limits as required per USPO-5217. The total particulates (per m^3) data collected for (b) (4)
(b) (4) (b) (4) did not meet the prospective acceptance limits for the (b) (4) Grade (b) (4) classification. Specifically, (b) (4) instances of total particulates exceeding the alert level of (b) (4) should have triggered alert level excursions.

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b. You utilize (b) (4) to downgrade Grade (b) (4) suite to Grade (b) (4) status. The instructions of the form indicate to conduct activities in accordance (b) (4) (b) (4) However, (b) (4) does not exist in (b) (4) and your firm failed to explain what document and section were reviewed to enable return to service.

c. You provided Environmental Monitoring data package collected on May 17, 2025, used to restore the Grade (b) (4) status of (b) (4) However, the EM data contained numerous samples with "N/A" readings which lacked applicable testing results.

d. Control of electronic data captured on the (b) (4) computerized system supporting restoration of Grade (b) (4) is deficient. For example:

i. (b) (4)

ii.

OBSERVATION 9

Each batch of drug product purporting to be sterile and/or pyrogen-free is not adequately tested to determine conformance to such requirements. Specifically, sterility samples of CASGEVY drug product are stored frozen under liquid nitrogen per procedure USPO-30461 titled (b) (4) Analytical Testing - QC Monograph for (b) (4) Product Samples", and shipped in liquid nitrogen prior to sterility testing.

OBSERVATION 10

Pest control program is deficient. The pest control trending report for Q1 2025 indicated numerous incidences of insects (same type) in (b) (4) and Grade (b) (4) storage room (b) (4) which are (b) (4) corridor and Grade (b) (4) corridor, respectively. The same insect species was reported to be persistently seen in the facility with incidences varying seasonally. No source for the insect entry has been identified, and no deviation has been initiated.

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***DATES OF INSPECTION**
06/02/2025 (Mon) through 06/06/2025 (Fri)

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