

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

<small>DISTRICT ADDRESS AND PHONE NUMBER</small> FDA/CDER/OPQ/OPMA/Division of Biotechnology Manufacturing  10903 New Hampshire Avenue, Silver Spring, MD 20993 Email: OPMABLAInspection483Responses@fda.hhs.gov	<small>DATE(S) OF INSPECTION</small> 10/20/2025-10/28/2025
	<small>FEI NUMBER</small> 3002930340

<small>NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED</small> Mr. Claudio Cescato, Ph.D., Head of Quality, Lonza Visp	
<small>FIRM NAME</small> Lonza AG	<small>STREET ADDRESS</small> Lonzastrasse 2
<small>CITY, STATE, ZIP CODE, COUNTRY</small> CH-3930 Visp, Switzerland	<small>TYPE ESTABLISHMENT INSPECTED</small> 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 WE OBSERVED:


**OBSERVATION 1**

The information provided by the firm does not conform to the (b) (4). Specifically, in the (b) (4) the (b) (4) drug substance (DS) shelf life is (b) (4) at  $\leq$  (b) (4) °C. However, the shelf life applied to DS Process Performance Qualification (PPQ) batches (Batch (b) (4)) and post-PPQ batches (Batch (b) (4)) was (b) (4).

**OBSERVATION 2**

The (b) (4) (b) (4) integrity test procedure used for the (b) (4) does not follow the vendor recommendations (document (b) (4) version (b) (4) or SOP CHVI-346656 v2.0 “(b) (4) Operation of (b) (4) and Integrity Test of (b) (4)”). For example:

- a. (b) (4) version (b) (4) indicates to (b) (4) for test set-up. However, the (b) (4) for test set-up is in (b) (4) per SOP CHVI-346656 v2.0 Figure (b) (4). The (b) (4) according to the guidance shown in the (b) (4) Manufacturing Executing System (MES) guidance for the operators.
- b. (b) (4) version (b) (4) indicates that the (b) (4) should be (b) (4). This step is not included in SOP CHVI-346656 v2.0 or in the (b) (4) MES guidance for the operators.
- c. (b) (4) version (b) (4) indicates to observe and disregard (b) (4) that occur in the (b) (4) (waiting time), and to observe the (b) (4) for (b) (4) (observation time).
  - i. The (b) (4) MES instructions indicate to start the timer immediately after the (b) (4) is (b) (4) and conduct the test for (b) (4) (observation time) without mentioning any waiting time (MES instruction paths (b) (4)).

SEE REVERSE OF THIS PAGE	<small>EMPLOYEE(S) SIGNATURE</small> 	<small>EMPLOYEE(S) NAME AND TITLE (Print or Type)</small> Reyes Candau-Chacon, PhD, Microbiologist Ralph M. Bernstein, Ph.D., Biologist Lei Zhang, Ph.D., Lead Biologist Alexander Sohr, Ph.D., Pharmaceutical Scientist	<small>DATE ISSUED</small> 10/28/2025
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- ii. SOP CHVI-346656 v2.0 step (b) (4) includes an observation time of (b) (4) or more without mentioning any waiting time.
- d. (b) (4) version (b) (4) indicates that the integrity test passes if there is (b) (4)
- (b) (4) The (b) (4) MES guidance for the operators indicate that the integrity test passes if (b) (4)

**OBSERVATION 3**

Process Parameters (PPs) are not adequately controlled within established ranges in (b) (4) DS manufacturing process. Specifically, PP deviations occurred during (b) (4) post-PPQ Batch (b) (4) and Batch (b) (4) manufacturing, including deviations for Critical Process Parameters (CPPs). In addition, Batch (b) (4) and Batch (b) (4) had out-of-specification (OOS) and borderline results, respectively, for (b) (4) (b) (4) assay at release. The CPP deviations observed include:

- a. (b) (4) batch (b) (4) outside proven acceptable range on (b) (4) Stage): during (b) (4) of production (b) (4) step for Batch (b) (4) (a CPP) was (b) (4) which was below the PAR of (b) (4) and NOR of (b) (4) for (b) (4)
- b. (b) (4) Batch (b) (4) and (b) (4) exceedance for (b) (4) as per CHVI-626612): during (b) (4) manufacturing for Batch (b) (4) and Batch (b) (4) had (b) (4) of (b) (4) respectively which exceeded the  $\leq$  (b) (4) limit, and (b) (4) had (b) (4) of (b) (4) which exceeded the  $\leq$  (b) (4) limit. (b) (4) for (b) (4) and (b) (4) are CPPs.
- c. (b) (4) Batch (b) (4) Excursion of (b) (4) during (b) (4) during the (b) (4) step for Batch (b) (4) the (b) (4) was reported as (b) (4) and the acceptable range is (b) (4) (b) (4) is a CPP for the (b) (4) step.

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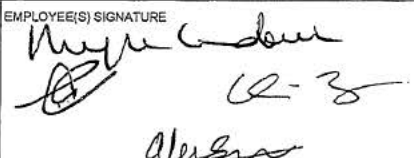
Batch (b) (4) had OOS (b) (4) result of (b) (4) % at release, which is below the specification limit of (b) (4) (b) (4) %. Batch (b) (4) had (b) (4) result of (b) (4) % at release, which is a borderline result that falls just above the lower specification limit (b) (4) Batch (b) (4) assay OOS on (b) (4) sample, due date: (b) (4)

**OBSERVATION 4**

Critical material used to manufacture (b) (4) is not tracked, maintained, or replaced throughout their lifetime. Specifically:

- The (b) (4) Integrity Tester used for (b) (4) including the (b) (4) (b) (4) DS (b) (4) has a (b) (4) (SAP No: (b) (4) installed between the (b) (4) to avoid (b) (4) from the product (b) (4) entering and damaging the instrument. The (b) (4) is not tracked or maintained and is replaced only when damaged. During the FDA inspection of the (b) (4) integrity test execution on October 24, 2025, a (b) (4) coming from the (b) (4) through the (b) (4) reaching approximately (b) (4) Impact of the (b) (4) in the results of the (b) (4) integrity test cannot be discarded.
- The (b) (4) instrument used to seal (b) (4) drug substance bags does not have a unique tracking number, and is not maintained or calibrated.
- The (b) (4) used for the (b) (4) or for the (b) (4) (b) (4) do not have a preventative maintenance program. The product contact part of the (b) (4) is (b) (4) and replaced (b) (4) however, maintenance of the (b) (4) (b) (4) of the (b) (4) is "failure-based" (they are used until they fail, and then they are replaced by a working (b) (4) The facility has a single spare (b) (4) to be used as replacement for the (b) (4) (b) (4) used for (b) (4) at the time of the inspection, there was no available working (b) (4) compatible with the (b) (4) used for (b) (4) because the only spare (b) (4) had a (b) (4) (b) (4) failure and was being repaired since July 9, 2025; a new (b) (4) for the (b) (4) was ordered on October 28, 2025.

**DATES OF INSPECTION:** 10/20/2025 (Mon), 10/21/2025 (Tues), 10/22/2025 (Wed), 10/23/2025 (Thurs), 10/24/2025 (Fri), 10/27/2025 (Mon), 10/28/2025 (Tues)

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