DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
CDER/OPQ/OPMA/Division of Pharmaceutical Manufacturing Assessment VI 10903 New Hampshire Avenue; White Oak Building 51, Room 2269 Silver Spring, MD 20993 E-mail: opmablainspection483responses@fda.hhs.gov	09/08/2025-09/19/2025
	FEI NUMBER 3010977634
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED Chandrakant Kathote, Site Head & Sr. Vice President- Operations	
FIRM NAME Lupin Limited (Biotech Division)	STREET ADDRESS Gat No. 1156, 1157, 1158, 1159 and 1160, Village-Ghotawade, Taluka-Mulshi
CITY, STATE, ZIP CODE, COUNTRY Pune, Maharashtra, 412115, India	TYPE ESTABLISHMENT INSPECTED Drug substance and 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

There are no written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess. Specifically,

A. The resumption of the filling activity after stoppage is not adequate. According to the current Batch Processing Record for Manufacturing, if machine stoppage occurs for (b) (4) or less, there is no (b) (4) (b) (4) of the line.

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B. The (b) (4) frequency is not adequate. The current Batch Processing Record for Manufacturing instructs operators to perform (b) (4) (b) (4) if machine stoppage exceeds (b) (4)

C. Your manufacturing process is not adequately validated. Per SOP_(b) (4)_DP_030999, Version 12.0, effective on September 05, 2025, Section 5.13, the (b) (4) process of the (b) (4) drug product (b) (4) can be carried out up to (b) (4) times. However, you did not perform appropriate validation to support this (b) (4) process.

D. Your manufacturing process lacks adequate control. On September 15, 2025, during the packaging operation of (b) (4) drug product (Batch# (b) (4) on the packaging machine (b) (4) that is also used for (b) (4) drug product (b) (4) packaging, water drops on the (b) (4) side of the sealed (b) (4) were observed on the conveyer belt where the packaged (b) (4) were collected into the (b) (4) Within less than one minute (12:16 PM), at least three units with water drops on the (b) (4) were observed. The water drops were from (b) (4) of the (b) (4) on the

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packaging machine that is used to [redacted] At the scene, one operator stopped the packaging line and wiped the [redacted] and then resumed the line. This operation is not described in SOP_[redacted]_DP_030999, Version 12.0, Procedure for Packing Operations in Drug Product Manufacturing.

OBSERVATION 2

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

A. On September 10, 2025, during aseptic filling operation performed in Filling Room [redacted] (Grade B environment), Building [redacted] for [redacted] drug product (Batch # [redacted] the operator while [redacted] the Restricted Access Barrier System (RABS, Grade A environment), sanitized and cut a strip of the external surface of the [redacted] bags containing the [redacted] and then inserted the [redacted] into the filling line. During the operation, the operator repeatedly inserted a portion of the open bag that was not sanitized into the RABS. Per Batch Product Record of [redacted] Doc No. [redacted] the filling ended at [redacted] on September 10, which is more than [redacted] from the beginning of the last sanitization of the whole external surface of the [redacted] bags performed on the unloading side (Grade B environment) of [redacted] ocated outside Filling Room [redacted] per ANNEX_[redacted]_DP_033054 Material Transfer Record.

B. Written procedures are lacking for the use of cleaning and sanitizing agents to prevent the introduction of microbial contamination into controlled manufacturing environments used for the manufacture of drug products in the facility. Specifically, efficacy studies have not included [redacted] the material type for the [redacted] bags and the [redacted] around the [redacted] for the [redacted] disinfectants used at the facility [redacted] The [redacted] around the [redacted] was observed entering the RABS (Grade A) at the time of introduction of the [redacted] into the RABS during the [redacted] drug product filling on September 10, 2025. Prior to September 17, 2025, the disinfectant efficacy studies had not

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included (b) (4) the material type for the RABS conveyor belt for the (b) (4) disinfectants used at the facility.

C. (b) (4) operators perform the installation of the (b) (4) in the RABS after cleaning of the RABS and before setup of the filling line. In a video for the installation of the (b) (4) in the RABS, the operator was observed inserting his (b) (4) hand and arm into the (b) (4) of the (b) (4) Following the installation of the (b) (4) on (b) (4) the operators proceed directly to (b) (4) Integrity Testing, which takes approximately (b) (4) and perform personnel monitoring upon exit from Grade B after this activity. The (b) (4) operators do not complete personnel monitoring directly after installation of the (b) (4)

D. The (b) (4) moves the (b) (4) from the conveyor belt to the (b) (4) It remains in the RABS and is not sterilized. The (b) (4) is directly over the open (b) (4) and blocks first air over the (b) (4) during filling. However, SOP_(b) (4)_QC_026625, Environmental Monitoring in Drug Product Manufacturing Facility, Version 15.0, effective April 10, 2025, provided insufficient instructions for operators to perform the monitoring of the (b) (4) and did not consider its entire surface for microbial swab testing.

OBSERVATION 3

The visual inspection procedures for sterile liquid drug products do not provide adequate assurance that finished products manufactured at the facility possess their purported quality attributes, including that they are essentially free from particulate matter. Specifically,

A. SOP_(b) (4)_DP_029538, Version 11.0, effective July 12, 2025, instructs Visual Inspection (VI) operators to hold (b) (4) units (b) (4) and inspect them against the (b) (4) (b) (4) background for not less than (b) (4) However, during the visual inspection of (b) (4) (b) (4) mg/(b) (4) mL (b) (4) for Batch (b) (4) on September 12, 2025, (b) (4) operators were observed performing the visual inspection of (b) (4) without knowledge of time in visual inspection booths (b) (4) The time spent on the visual inspection of the (b) (4) appeared to be inconsistent for (b) (4) (b) (4) and during the inspection on (b) (4) the (b) (4)

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background. Operator (b) (6) was timed at (b) (4) during the inspection of (b) (4) from (b) (4) on the (b) (4) background and the inspection lasted (b) (4)

B. On September 12, 2025, while performing the 100% VI on the (b) (4) the VI operator in (b) (4) did not hold the (b) (4) test units and reference standard (b) (4) vertically for fill volume check per Section 5.3.15.2 of SOP (b) (4) _DP_029538, Version 11.0, effective July 12, 2025.

C. For (b) (4) check during VI, the (b) (4) test units and reference standard (b) (4) are (b) (4) (b) (4) which could introduce variability in determining the (b) (4) as the units are not levelled.

OBSERVATION 4

Standard operating procedures and protocols are not followed, established, or adequate. Specifically,

A. SOP (b) (4) DP_028978, Procedure for Aseptic Machine Parts Assembly, Handling, Tracking and Trending of Aseptic Interventions, Version 17.0, effective on September 3, 2025, is not adequate. On September 9, 2025, during (b) (4) process conducted in Room (b) (4) Building (b) (4) the supporting operator standing on one side of the LAF, sanitized the hands and forearms by spraying (b) (4) each time. The spraying was close to the exposed settle plate placed on the LAF (b) (4) and could potentially contaminate the settle plate and cause false negative results. The provided training record indicated that the operator was trained based on the above mentioned SOP where Section 5.1.10 has a note stating "Ensure that the personnel in filling area perform hand sanitization away from the expose environmental monitoring plates". The instructions are inadequate for operators to perform the hand sanitization while avoiding the potential contamination of the exposed settle plates.

B. Written procedures are not adequate to prevent contamination during drug substance (b) (4) The same pair of sterile forceps was used multiple times to (b) (4) used for drug substance (b) (4) (b) (4) (b) (4) per SOP (b) (4) _DP_029584, Aseptic Operations in Drug Product Manufacturing Area, Version 14.0, effective September 8, 2025, under LAF EPQ/DPD/016, in Room (b) (4) (Formulation Room), on September 9, 2025. The process was repeated for (b) (4) DS (b) (4) and

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the portion of the (b) (4) tubing that was contacted by the forceps, which touched multiple surfaces, was (b) (4) When the forceps contacted the (b) (4) tubing of the (b) (4) assembly to (b) (4) it had previously contacted at least eight surfaces.

C. During (b) (4) of the (b) (4) drug substance, (b) (4) of sterile forceps are used. (b) (4) The (b) (4) forceps was used at least six times during the (b) (4) activities. SOP (b) (4) _DP_029584 does not provide sufficient details to operators regarding which (b) (4) forceps to use at each step to prevent contamination of the (b) (4) tubing of the (b) (4) assembly that (b) (4)

D. Section 5.8.12 of SOP_(b) (4) Procedure for (b) (4) Management in Drug Product Manufacturing, Version 5.0, effective April 18, 2025, included a pictorial representation of the Filling Room operator removing the (b) (4) of the (b) (4) exposing the (b) (4) to the Grade B environment prior to its introduction in the RABS. Section 5.8.5 of SOP_(b) (4) _DP_030613, Procedure for (b) (4) Management in Drug Product Manufacturing, Version 6.0, effective September 9, 2025, instructs operators to start unloading of (b) (4) from (b) (4) LAFU and remove the (b) (4) of (b) (4) n support LAFU and (b) (4) (b) (4) There are insufficient instructions in the current version of SOP_(b) (4) _DP_030613 for operators to prevent the exposure of the (b) (4) of the (b) (4) to the Grade B environment during the introduction of the (b) (4) in the RABS.

E. SOP_(b) (4) _QC_026625, Environmental Monitoring in Drug Product Manufacturing Facility, Version 15.0, effective April 10, 2025, states the operator should keep the sanitized plate on settle plate (b) (4) without touching plate with (b) (4) In preparation for the introduction of settle plates into the RABS at (b) (4) on September 10, 2025, the QC operator's (b) (4) fingers touched a settle plate in Grade B while holding the settle plate with a wipe.

F. SOP_(b) (4) 025672, Decontamination of Materials, Version 3.0, effective on September 13, 2024, is not followed or adequate.

i. Your manufacturing staff did not follow the procedure per Section 5.7.1 to decontaminate the collected (b) (4) from the (b) (4) during the (b) (4) process. The procedure requires (b) (4) for

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the decontamination. You indicated that no measurements were performed, and addition of [(b) (4)] was not recorded. The [(b) (4)] was collected in an open bag contained in an open container that was unlidded.

ii. Section 5.7.1 of SOP_[(b) (4)]025672 did not describe the minimum contact time of [(b) (4)] and the [(b) (4)] before the [(b) (4)] is [(b) (4)]

G. Your decontamination process of the collected [(b) (4)] is not adequately validated. You did not perform appropriate studies to verify the effectiveness of the decontamination process of the [(b) (4)] as described in SOP_[(b) (4)]_MI_025672, Decontamination of Materials, Version 3.0, effective on September 13, 2024.

H. Your sampling operation is inadequate. For example, at the end of [(b) (4)] of the drug substance operation performed in Room [(b) (4)] Formulation Room for [(b) (4)] drug product (Batch # [(b) (4)] mg [(b) (4)] mL), during the sampling operation, the solution kept dripping from the pipette onto multiple equipment surfaces throughout the whole transfer process.

I. Your disinfection / sanitization operation on the manufacturing floor is inadequate. For example, on September 12, 2025, during the [(b) (4)] collection process, one collection bottle containing residual [(b) (4)] fell down on the bench of the laminar air flow cabinet, the operator picked up the bottle and resumed the collection operation of the remaining [(b) (4)] bottles on the same spot without cleaning the possibly contaminated surface. This might cause cross contamination of the other bottles and subsequently all the surfaces being contacted by the bottles post-collection since no further cleaning of the bottles was performed after the collection was completed in the LAF and the bottles moved out of the LAF to a [(b) (4)]

J. Your facility maintenance is inadequate. For example, on September 10, 2025, there was dried up [(b) (4)] on the inner surface of the [(b) (4)] portion of the [(b) (4)] located in [(b) (4)] Room [(b) (4)] Building [(b) (4)] There were [(b) (4)] pieces stuck onto the [(b) (4)] [(b) (4)] There was dirt and stagnant liquid noted on the [(b) (4)] of the [(b) (4)] portion [(b) (4)] Solids and dirty stagnant liquid were also noted from [(b) (4)] located in [(b) (4)] Room [(b) (4)]

K. The periodic observation of cleaning of the RABS by Quality Assurance is not operationalized and documented.

L. [(b) (4)] in the [(b) (4)] is used for the transfer of materials and product into the drug product manufacturing area corridor (Grade D). The two logbooks in the

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(b) (4) Material Transfer Record (For loading side, Annex_(b) (4)_DP_033054) and Usage and Intactness Check Record of Pre-Sterile Material (Annex_(b) (4)_DP_026873), had no written documentation of the periodic review by Quality Assurance. The (b) (4) of (b) (4) (b) (4) was not fully aligned during the walkthrough and needed repair.

M. SOP_(b) (4)_QC_026780, Good Chromatographic Practices and Documentation, Version 13.0, effective August 29, 2025, notes that the checklist for liquid chromatographic analysis should be filled before initiation of analysis as per Annex_(b) (4)_QC_026787. It notes that the checklist shall be filled by an analyst and be verified by trained analyst or reviewer. However, self-verification by the analyst is also permissible to initiate the sequence in the absence of a reviewer.

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