DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	9/8/2025-9/16/2025*
	FEI NUMBER 3015392060

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Ranjana Pathak, President & Chief Quality Officer Corporate Quality Assurance

FIRM NAME	STREET ADDRESS
Lupin Limited	Unit -2 Plot No. 6B, Sector-17, Special Economic Zone, Mihan
CITY, STATE, ZIP CODE, COUNTRY Nagpur, Maharashtra, 441108 India	TYPE ESTABLISHMENT INSPECTED Sterile 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
Procedures designed to prevent microbiological contamination of drug products purporting to be sterile did not include adequate validation of the aseptic and sterilization process.

Specifically,

A. Your firm's qualification of airflow in critical areas is insufficient to evaluate unidirectional airflow, contamination risk, and aseptic processing line suitability due to the smoke studies being performed using (b)(4) smoke generated via (b) (4) This smoke is not neutrally buoyant, potentially masking the true airflow pattern and making it difficult to identify issues like recirculating air or dead spots.

Additionally, the following discrepancies were noted in some interventions:

1. The angle of video recording does not include the full range of air flow, for example from the top of the (b) (4) to the (b) (4)
   - (b) (4) Removal of fallen vial/jam vial at (b) (4) assembly video, vial filling line, 20Oct2023
   - (b) (4) Adjustment of (b) (4) assembly at loading, unloading station video, vial filling line, 20Oct2023
   - (b) (4) Removal of fallen vial/jammed vial from auxiliary conveyor 1 video, vial filling line, 20Oct2023
2. All activities are not represented, including the retrieval of scissors and forceps or the consolidation of trash after assembly of the (b) (4)
   - (b) (4) Fixing of (b)(4) into (b) (4) fixing another end of (b)(4) tubing in (b) (4) of (b) (4) vessel video, vial filling line video, 15Jan2025 (forceps)
   - (b) (4) Environmental monitoring video, (b) (4) line, 15Jan2025, (scissors)
   - (b) (4) Placement of stopper in (b) (4) filling line video, 15Jan2025, (forceps)
   - (b) (4) Removal of fallen vial/jammed vial from auxiliary conveyor 1 video, vial filling line,

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20Oct2023 (forceps)

- 2025 Removal of the (b) (4) of (b) (4) using sterile forceps video, vial filling line, 04Sep2025, (consolidation of trash)

3. The amount of smoke is not adequate to evaluate activities such as insertion of arms into the (b)(4) (b) (4)
   - (b) (4) Fixing of (b)(4) into (b) (4) fixing another end of (b)(4) tubing in (b) (4) of (b) (4) vial filling line, 15Jan2025
   - (b) (4) Adjustment of tubing at (b) (4) hose (b) (4) filling line, 15Jan2025
   - (b) (4) Replacement of (b) (4) vial filling line, 15Jan2025
   - (b) (4) Placement of stopper in (b) (4) filling line, 15Jan2025
   - (b) (4) Replacement of (b) (4) 15Jan2025

B. Your firm's (b)(4) validation load patterns for the (b) (4) ID No. (b)(4) is inadequate, in that:

1. A risk assessment to identify worst-case locations for (b) (4) biological indicator placement within the sterilization load configurations could not be provided. During review of your (b)(4) load pattern validation documentation the following was noted
   - (b) (4) biological indicators were placed on the outside surface of clean room wipes rather than in the center where (b) (4) would be most challenging.
   - Tubing was cut to accommodate (b) (4) placement, biological indicator placement which negates the ability to determine the effectiveness of (b) (4) throughout the length of the tube
   - For small diameter tubing, the tubing is (b) (4) (b) (4) This setup does not represent the actual sterilization conditions of intact product packaging.
   - For (b) (4) tubing, (length of (b) (4) inner diameter (b) (4) was not evaluated to ensure sterility.
   - Biological indicators (b) (4) were placed in bags with closed (b)(4) scissors but positioned outside the scissor blades rather than between the closed blades where (b) (4) would be most challenging.

2. (b)(4) bags with (b) (4) were used without documentation demonstrating suitability for (b) (4)

(b) (4) sterilization. No documentation was provided specifying the type of (b) (4) used during the assembly of the bags at the supplier. Additionally, validation data was not provided to show that the (b) (4) which represent the most challenging location for (b) (4) achieve sterility during the sterilization process.

C. Aseptic qualification of personnel who perform activities inside the aseptic processing (b) (4) that may have direct impact on the sterility assurance of the product are classified as Category A.

1. (b) (4) line and the Vial line (b) (4) the (b) (4) with the setup of the filler, making it unclear who performs which operation. As multiple people are documented as performing this one intervention, the lack of distinction results in personnel who perform the (b) (4) the (b)(4) being qualified to setup the filling machine during a media fill.

2. It is unknown if Category A personnel met the requirements described in the "Rationale of Interventions for Personnel Qualification/Requalification in Media Fill – (b) (4) " as the "Intervention Tracking in Media Fill" form used to track qualification activities since 29Aug2023, inadvertently did not list all interventions required by the rationale. This discrepancy was not corrected until 05Sep2025. A retrospective evaluation was not performed on the Category A personnel for the (b)(4) line to determine the impact of this error and instead the Rational of Interventions document was updated to remove the need to perform the missing intervention.

D. The (b)(4) qualification studies for your (b) (4) including the (b)(4) (Equipment ID: (b)(4)) and (b)(4) (Equipment ID (b) (4)) conducted in (b) (4) failed to demonstrate that biological indicator placements represent the most challenging conditions for (b) (4)

1. No risk assessment could be provided to show the current BI locations used during (b) (4) decontamination of the (b) (4) are worst case.

   On 11 Sep 2025, we observed your (b) (4) setup for your (b)(4) (Equipment ID (b) (4) (b)(4)) the following discrepancies were noted.

   - The edge of the (b) (4) was placed on top of the (b) (4) cover during the (b) (4) cycle. No BI was placed between the two pieces of equipment to show (b) (4) Referencing

your qualification studies from (b) (4) revealed that these areas were not identified as potential challenging conditions for (b) (4) despite the complex geometries created by these surface-contacting areas.

- Numerous surface contacting equipment parts were identified during the (b) (4) decontamination process for (b) (4) bags were observed touching together and contacting other surfaces (b) (4) and equipment parts). Your qualification studies from (b) (4) lacked a risk assessment to identify these surface contacting areas as representing the most challenging conditions for (b) (4)

2. Your procedures (SOP_NG 2_PR_017941 and SOP_NG 2_PR_020134) state prior to (b) (4) decontamination, "Arrange the material in such way that it should not fall down or having minimum touch to each other during the decontamination", without defining the definition of "minimum touch" and how "minimum touch" will affect the (b) (4)

E. Initial qualification of new container sizes on the (b)(4) and the Vial lines are deficient in that all required interventions are performed in (b) (4) out of the (b) (4) executed batches. The remaining (b) (4) batches only execute the amount of interventions to qualify Category A personnel. This applies to all initial qualification of a new container size. Recently executed examples include:

- Initial qualification of (b)(4) executed in Media Fill Simulation Study for (b) (4) on (b) (4) This qualification would be in support of the aseptic filling of (b) (4) Injection (b) (4) mg/mL and (b) (4) mg/mL (b) (4)

- Initial qualification of (b)(4) executed in Media Fill Simulation Study for Vial Filling Line on (b) (4) This qualification would be in support of the aseptic filling of (b) (4) Injection, USP (b) (4) mg/mL (b) (4)

OBSERVATION 2
Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established, written and followed.

Specifically,

A. Interventions which occur during commercial manufacturing are not tracked or trended per container size. Instead,

interventions for all vial sizes (b) (4) are grouped together resulting in changes occurring within a specific container size not being detected.

B. The following discrepancies were noted during the review of visual inspection procedures:

Black particles, white particles and fibers are categorized as major defects without adequate scientific justification. The Rational for Defects of Visual Inspection Categorized as Critical, Major & Minor states depending on the nature of the white particle, black particle, and fiber, it could potentially harm patients. To date, no identification of fibers and black or white particles have taken place to determine if the source of these particles are intrinsic or extrinsic.

OBSERVATION 3
Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically,
Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

A. Non-viable particle counter (NVPC) tube lengths in your (b) (4) Filling Line and Vial Filling Line exceeded (b) (4) meter without evaluation of particle loss. Specifically, installation measurements for the (b) (4) Filling Line NVPCs were (b) (4) meters, while your provided measurements showed (b) (4) meters. Additionally, a (b) (4) NVPC added to your Vial Filling Line measured (b)(4) meters during installation but (b)(4) meters per your documentation.

B. According to your "Non-Viable Particle Counter Tube Length and Bend Verification Study," dated 07Mar2018, the installation contractor used a cardboard template, cut to an approximate (b) (4) mm radius, as the measuring device. Cardboard is not a calibrated or verified measuring tool.

OBSERVATION 4
There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has been already distributed.

Specifically,
Your quality unit failed to investigate the root cause of the biological indicator failure at position (b) (4) (b)(4) ", where BI (b) (4) showed growth while BI (b) (4) did not. The (b)(4) qualification report of (b)(4) for (b)(4) (b) (4) (Equipment ID (b) (4) dismisses this failure by stating that "occasional growth of

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(b) (4) BI out of (b) (4) BIs may consider valid as it is evident that, BIs are having inherent property of variability." This statement lacks scientific rigor because the (b) (4) BIs were not placed in the same location. Instead, these BIs were placed in between different (b) (4) The evaluation did not take into account the (b) (4) and the effect on (b) (4) The absence of investigation into these critical factors represents a failure to determine whether this was a true process failure, a documentation/positioning issue, or a rogue BI.

Additionally, neither the protocol nor the report identifies the exact location of the failed (b) (4) BI.

OBSERVATION 5

Appropriate controls are not exercised over computers or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel.

Specifically,
During review of the document control system, (b) (4) documents were identified as standalone. These documents do not have any linkage to SOPs and do not go through change control upon revision. The topics of these documents regard the bracketing approach rationale for periodic media fill simulation studies, rationale of interventions performed for personnel qualification/requalification in vial and (b) (4) line, rationale for bracketing approach in visual inspector qualification, rationale for defects of visual inspection categorized as critical, major & minor for (b) (4) (b)(4) defects, (b) (4) product vials, location and rationale for NVPC of sterility testing (b) (4) rationale for microbiological sampling and analysis of (b)(4) and (b)(4) from product processing area (production and warehouse).

Eleven (11) gap assessments were identified which are not integrated into a Quality System (i.e., CAPA or investigation procedure). Changes to a gap assessment do not go through change control. Only corrective actions generated as a result of the gap assessment are handled through CAPA/change control.

Electronic templates are initially controlled and issued by quality but once issued, the receiver could reuse that template indefinitely. Templates are used during trending, quality risk assessments, lists of authorized personnel, and gap assessments. Executed templates are not given revision numbers and do not go through change control.

OBSERVATION 6

The written stability program for drug products does not include reliable, meaningful and specific test methods.

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Specifically,

A. SOP MUM CQA 021145 Validation of Analytical Method for Drug Product procedure states about (b)(4) % degradation shall be achieved in any one of stress conditions with mass balance. If (b)(4) % degradation cannot be achieved, scientific justification shall be provided. This results in lack of justification for not obtaining (b)(4) % degradation in any remaining stress condition once one condition is met. For example,

- (b)(4) % degradation was not achieved execution of Forced Degradation Report for the Test of Assay and Degradation Products of (b)(4) in (b)(4) Injection USP (b)(4) Injection (b)(4) (b)(4), and thermal conditions without justification.
- (b)(4) % degradation was not achieved during execution of Forced Degradation for the Test of Assay, Degradation Products Method (b)(4) Degradation Products Method (b)(4) (for (b)(4) (b)(4) and Degradation Products Method (b)(4) (for (b)(4) in (b)(4) Injection by HPLC for acid, oxidative, thermal, and photolytic conditions without justification.
- (b)(4) % degradation was not achieved during execution of Forced Degradation for the Test of Assay, Degradation Products Method (b)(4) and Degradation Products Method (b)(4) (for (b)(4) Impurity) in (b)(4) Injection USP for oxidative, thermal, and photolytic conditions without justification.
- (b)(4) % degradation was not achieved during execution of Forced Degradation Study of Degradation Products (Method (b)(4) and Method (b)(4) and Assay for (b)(4) Injection USP for acid, (b)(4), thermal, and photolytic conditions without justification.

B. Mass balance was not achieved during photolytic degradation condition in the Forced Degradation Report for the Test of Assay and Degradation Products of (b)(4) in (b)(4) Injection USP (b)(4) Injection. Data could not be provided to demonstrate the degradation method is stability indicating.

***DATES OF INSPECTION**
9/08/2025(Mon), 9/09/2025(Tue), 9/10/2025(Wed), 9/11/2025(Thu), 9/12/2025(Fri), 9/15/2025(Mon), 9/16/2025(Tue)

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Nagpur, Maharashtra, 441108 India	Sterile Manufacturer

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