

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/8/2018-10/18/2018*
	FEI NUMBER 3009107538

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED  
Amit Sareen, Site Head and Vice President-Manufacturing

FIRM NAME Lupin Limited	STREET ADDRESS Unit 3, Plot No. M-1, Sez, Phase Ii, Misc Zone, Apperal Park, Dist Dhar
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CITY, STATE, ZIP CODE, COUNTRY Pithampur, Madhya Pradesh, 454775 India	TYPE ESTABLISHMENT INSPECTED Drug Manufacturer
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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 I OBSERVED:**  
Drugs

**OBSERVATION 1**

Control procedures are not established which monitor the output and validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product.

Specifically,

- a) your process performance qualification (PPQ) study is deficient in that you did not include the second exhibit batch for (b) (4) mg, lot # (b) (4) which failed (b) (4). You rejected this batch and did not include it in your PPQ report.

During the inspection, you stated this batch was a product development batch manufactured before exhibit batches and production process is recorded in PD notebooks. When I asked for the production records and copies of the PD notebooks, you stated that this batch was the first exhibit batch and failed (b) (4). Review of your SAP records showed that this batch was the second exhibit batch, then you admitted that this batch was the second exhibit batch which failed (b) (4) and you rejected the batch.

<b>SEE REVERSE OF THIS PAGE</b>	EMPLOYEE(S) SIGNATURE Yasamin Ameri, Chemist/Biologist	Yasamin Ameri Chemist/Biologist Signed By: 201565939 Date Signed: 10-18-2018 04:13:36 X	DATE ISSUED 10/18/2018

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b) additionally, after observing 1 out of (b) (4) (b) (4) failed the (b) (4) weight in exhibit batch # (b) (4) instead of investigation and more data, you revised the exhibit batch record and removed (b) (4) weight measuring" requirement.

**OBSERVATION 2**

Written procedures for cleaning and maintenance fail to include description in sufficient detail of methods, equipment and materials used, description in sufficient detail of the methods of disassembling and reassembling equipment as necessary to assure proper cleaning and maintenance and instructions for removal or obliteration of previous batch identification.

Specifically,

a) cleaning validation and verification for rooms and equipment used for (b) (4) (b) (4) filling, and (b) (4) of (b) (4) (b) (4) mg are deficient. You have not performed full cleaning studies on dedicated equipment and cleaning validation on production room # (b) (4) which is a multi-use room and is used for (b) (4) of (b) (4) (b) (4) as well as filling of (b) (4) and other potent drug products such as (b) (4) solutions, (b) (4) drug products, etc. to ensure preventing cross contamination and carry over.

You failed to provide a proper study and execution plan for validation and verification of the cleaning. During the inspection you stated you conduct Type (b) (4) cleaning, which is a (b) (4) (b) (4) for cleaning of equipment used in production of (b) (4) mg since they are dedicated equipment. Later, you stated you perform Type (b) (4) cleaning, which is a (b) (4) on production of (b) (4) (b) (4) mg even though they are dedicated equipment. On Tuesday Oct. 16, 2018 (two days before inspection closing day) you provided a series of data showing

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(b) (4) swab sample results for different production equipment for (b) (4) and stated you have done a few studies and determined the hold time for cleaned equipment.

b) your batch record for (b) (4) of (b) (4) is missing type of cleaning and cleaning instructions on (b) (4) unit and there is no computer station inside the (b) (4) room for the operator to access cleaning SOP electronically.

**OBSERVATION 3**

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,

- a) control over the computerized system in QC laboratory is deficient. Your QC laboratory Manager has permission to allow modification to the sequences in HPLC and GC systems. Your QC laboratory reviewer does not review the modification to the sequence after unlocking and change to the sequence. Your QC reviewer even stated that they do not investigate modifications to the sequences during normal review process and accepts the audit trail report as "sequence modified".

You stated that the unlocking permissions should be approved by QA and are kept in modified folder for that specific sequence. You failed to provide a copy of a modified sequence which is approved by QA. When I asked for traceability of the permissions you stated that the permission records are not traceable.

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b) your procedures (QCD-60, QCD61, and ITP-034) for control of computerized systems does not have instruction modification control over sequences in HPLC and GC and (b)(4) creation of folders standalone instrument such as FTIR, UV-Vis, etc. and locking of the folders at the (b)(4)

**OBSERVATION 4**

Sampling procedures are deficient regarding sampling components from the top, middle, and bottom of container.

Specifically, your sampling practice for removal of samples for APIs and (b)(4) is deficient in that you do not collect samples from different locations of material containers (top, middle and bottom). You use sampling (b)(4) for collecting samples of APIs which come in different size containers (b)(4) and (b)(4) from bags packed in a (b)(4) boxes.

Device

**OBSERVATION 5**

Procedures for acceptance of incoming product have not been adequately established.

Specifically, your procedure for receiving and inspection of (b)(4) is deficient in that you do not perform functional test on the received device before release the device for use. This device is used for delivery of (b)(4) ng.

**\*DATES OF INSPECTION**

10/08/2018(Mon), 10/09/2018(Tue), 10/10/2018(Wed), 10/11/2018(Thu), 10/12/2018(Fri),  
10/15/2018(Mon), 10/16/2018(Tue), 10/17/2018(Wed), 10/18/2018(Thu)

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**Annotations to Observations**

- Observation 1: Not annotated
- Observation 2: Not annotated
- Observation 3: Not annotated
- Observation 4: Not annotated
- Observation 5: Not annotated

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