

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

DISTRICT OFFICE ADDRESS AND PHONE NUMBER ORA OPQO HQ, 12420 Parklawn Drive, Room #2032 Rockville, MD 20857 email: ORAPHARMInternational483responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	DATE(S) OF INSPECTION 1/13/2020, 1/14/2020, 1/15/2020, 1/16/2020, 1/17/2020
	FEI NUMBER 3013127166

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED
TO: Abhijeet V. Shinde, Site Head and General Manager- Manufacturing

FIRM NAME Lupin Limited	STREET ADDRESS Plot 130, J.N. Pharma City, Road No. 11, Parawada Mandal
CITY, STATE AND ZIP CODE Visakhapatnam, Andhra Pradesh, 531019, India	TYPE OF ESTABLISHMENT INSPECTED API 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 (I) (WE) OBSERVED:

OBSERVATION 1

Critical process parameters should be controlled and monitored during process validation studies.

Specifically, process performance qualification studies on (b) (4) and (b) (4) are deficient in that your firm failed to:

a) identify the critical process parameters. The process performance qualification reports for these intermediates and API stated that you determined the quantity of raw materials such as (b) (4) or (b) (4) as the critical process parameters and process parameters such as (b) (4) as non-critical process parameters. For example,

- process performance qualification protocol and report for (b) (4) (PVP/MPP1/065/00) states the “Quantity of the (b) (4)” as the critical process parameter such as (b) (4) requirements for completion of the chemical reactions, as non-critical parameter

- process performance qualification protocol and report for (b) (4) (PVR/MPP1/063/00), states the “Quantity of (b) (4)” as the critical process parameters and parameters such as (b) (4) as non-critical parameters.

- process performance qualification protocol and report for (b) (4) (PVR/MPP1/068/00), states the “quantity of (b) (4)” as the critical process parameter and parameters such as (b) (4) requirements for starting or completion of chemical reactions as non-critical

Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Yasamin Ameri -S	EMPLOYEE(S) NAME AND TITLE (Print or Type) Yasamin Ameri, Investigator- DDC	DATE ISSUED 01/17/2020
	<small>Digital y signed by Yasamin Ameri S DN: cn=US, ou=US Government, ou=HHS, ou=FDA, ou=People, cn=Yasamin Ameri S, o=923421020030010011-2001565939, Date: 2020.01.17 02:10:32.0800</small>		

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

DISTRICT OFFICE ADDRESS AND PHONE NUMBER ORA OPQO HQ, 12420 Parklawn Drive, Room #2032 Rockville, MD 20857 email: ORAPHARMInternational483responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	DATE(S) OF INSPECTION 1/13/2020, 1/14/2020, 1/15/2020, 1/16/2020, 1/17/2020
	FEI NUMBER 3013127166

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED
TO: Abhijeet V. Shinde, Site Head and General Manager- Manufacturing

FIRM NAME Lupin Limited	STREET ADDRESS Plot 130, J.N. Pharma City, Road No. 11, Parawada Mandal
CITY, STATE AND ZIP CODE Visakhapatnam, Andhra Pradesh, 531019, India	TYPE OF ESTABLISHMENT INSPECTED API Manufacturer

parameters.

b) perform hold time studies during the critical processes and steps of the production. You only performed hold time studies on (b) (4) which is after the completion of all (b) (4) chemical reactions.

OBSERVATION 2

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

Specifically, during the production of exhibit batches and process performance qualification studies your firm failed to investigate the discrepancies observed in (b) (4) time for exhibit batches, instead you initiated a change control and revised the limits for (b) (4) nt in (b) (4) products from NMT (b) (4) % to NMT (b) (4) % for (b) (4) from NMT (b) (4) % to NMT (b) (4) % for (b) (4) API. For example, during the (b) (4) of the exhibit batches the results demonstrated that:

- the first exhibit batch of (b) (4) (batch (b) (4) was (b) (4) batch # (b) (4) was (b) (4) batch #s (b) (4) were (b) (4)

- the first exhibit batch of (b) (4) batch # (b) (4) was (b) (4) but second and third batches of (b) (4) exhibit batch #s (b) (4) were (b) (4) respectively.

- the first and second exhibit batches of (b) (4) batch #s (b) (4) exhibit batch # (b) (4) were (b) (4) but exhibit batch # (b) (4) (third batch) was (b) (4)

Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type) Yasamin Ameri, Investigator- DDC	DATE ISSUED 01/17/2020
--------------------------	-----------------------	--	---------------------------

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER ORA OPQO HQ, 12420 Parklawn Drive, Room #2032 Rockville, MD 20857 email: ORAPHARMInternational483responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	DATE(S) OF INSPECTION 1/13/2020, 1/14/2020, 1/15/2020, 1/16/2020, 1/17/2020 FEI NUMBER 3013127166
--	---

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED
TO: Abhijeet V. Shinde, Site Head and General Manager- Manufacturing

FIRM NAME Lupin Limited	STREET ADDRESS Plot 130, J.N. Pharma City, Road No. 11, Parawada Mandal
CITY, STATE AND ZIP CODE Visakhapatnam, Andhra Pradesh, 531019, India	TYPE OF ESTABLISHMENT INSPECTED API Manufacturer

OBSERVATION 3

Secondary reference standards should be appropriately prepared, identified, tested, approved, and stored.

Specifically, receiving and storage of secondary reference standards are deficient in that working reference standards that are:

- received from your (b) (4) are received with certificate of analysis and are not analyzed for identity and purity. For example, your firm has received (b) (4) vial of (b) (4) USP batch # (b) (4) from (b) (4) as working reference standard for analysis of (b) (4) API samples in June 2019. The QC records demonstrated that (b) (4) USP working standard is received and released for use with the analytical data and certificate of analysis. The QC laboratory failed to perform proper analyses on the secondary reference standards prior to release for use.

- not stored properly. For example, (b) (4) secondary reference standards such as (b) (4) USP or (b) (4) are stored in (b) (4) inside the QC cold storage (2°C -8°C) which is not controlled

OBSERVATION 4

Samples from incoming raw materials should be collected from top, middle, bottom of the raw material containers to represent the entire content of the container.

Specifically, raw material sampling process and procedure QCD-005-06, "Sampling", are deficient in that you neither have instruction for, nor collecting samples from top, middle, and bottom of raw material containers. For example, your firm has received (b) (4) of (b) (4) USP (b) (4) in 2018 for production of exhibit batches of (b) (4) Sampling (b) (4) ted that samples are collected only from th (b) (4) of the containers for chemical analysis.

Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type) Yasamin Ameri, Investigator- DDC	DATE ISSUED 01/17/2020
-----------------------------------	-----------------------	--	-------------------------------

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER ORA OPQO HQ, 12420 Parklawn Drive, Room #2032 Rockville, MD 20857 email: ORAPHARMInternational483responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	DATE(S) OF INSPECTION 1/13/2020, 1/14/2020, 1/15/2020, 1/16/2020, 1/17/2020
	FEI NUMBER 3013127166

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED
TO: Abhijeet V. Shinde, Site Head and General Manager- Manufacturing

FIRM NAME Lupin Limited	STREET ADDRESS Plot 130, J.N. Pharma City, Road No. 11, Parawada Mandal
CITY, STATE AND ZIP CODE Visakhapatnam, Andhra Pradesh, 531019, India	TYPE OF ESTABLISHMENT INSPECTED API Manufacturer

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, control over the creation, approval, and changes to the master batch records is deficient in that per the document No. QAD-026-01, "Preparation and filling of batch production records and equipment cleaning records", soft copy of the master batch record is controlled by the production department and all changes to the master batch records are made to the master batch record that is controlled by the production and not the QA document control.

There is no assurance that all changes to the master batch records are recorded and approved by the QA and there hasn't been an unauthorized change to the master batch record.

Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (<i>Print or Type</i>)	DATE ISSUED
		Yasamin Ameri, Investigator- DDC	01/17/2020