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 ORAPHARMInternational4@responses@fda.hhs.gov	11/14/2022-11/23/2022 FEI NUMBER 3002807511

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Rajendra B. Chamodkar, President Manufacturing Operations

FIRM NAME	STREET ADDRESS
Lupin Limited Unit I	Unit 1, 198-202 New Industrial Area No. 2
CITY, STATE, ZIP CODE, COUNTRY Mandideep, Madhya Pradesh, India-462046	TYPE ESTABLISHMENT INSPECTED Pharmaceutical 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:

DRUG PRODUCT OBSERVATION

OBSERVATION 1

There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Specifically,

a. On 11/16/2022, your Investigation Manager reviewed OOS/C/21/MDP/IPDP/002 that was initiated to probe an OOS result for a (b) (4)-point (b) (4) uniformity (b) (4) assay test for (b) (4) suspension (b) (4) CSP (b) (4) mg (b) (4) ml, Batch No. (b) (4). The OOS was reported for two sample locations including: (b) (4) (b) (4) %) and (b) (4) (b) (4) %) (Specification (b) (4) % - (b) (4) %). Although, Phase I and Phase II investigation did not reveal any assignable root cause, you proposed dilution error (not mixing the stock solution with the diluent) as the probable root cause. Through the hypothesis study, you also proved the dilution error as the root cause for the lower assay and retested the new sample and based on the passing results you invalidated the initial OOS result.

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12420 Parklawn Drive, Room 2032 Rockville, MD 20857 ORAPHARMInternational48@response@fda.hhs.gov	DATE(S) OF INSPECTION 11/14/2022-11/23/2022 FEI NUMBER 3002807511
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED Mr. Rajendra S. Chunodkar, President Manufacturing Operations	
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The aforementioned batch of (b) (4) was used to manufacture (b) (4) suspension (b) (4) (b) (4) USP (b) (4) mg (b) (4) ml. Batch No. (b) (4) This batch recorded OOS results for assay (stratified samples) at three points including (b) (4) %), (b) (4) %), (b) (4) (b) (4) (Specification (b) (4) % - (b) (4) %). On 11/16/2022, your Investigation Manager reviewed the respective investigation report OOS/C/21/ MDP/ IPDP/004. In Phase I investigation you noted the test failing for system suitability and through hypothesis test, you concluded instrument malfunction was the root cause for the recorded OOS results. You retested the sample and invalidated the initial OOS results.

The Head of Process Development and General Manager of Quality stated that the batch was part of monitoring study, and the batch disposition will be based on overall outcome of the study. However, under the normal circumstances, the batch would have been released based on the invalidated OOS results.

b. On 11/16/2022, your Investigation Manager reviewed OOS/C/20/MDP/FPDP/011 that was initiated to probe an OOS result for assay test for (b) (4) Capsule USP (b) (4) mg Batch No. (b) (4) The OOS was reported on the higher side and recorded as (b) (4) % (Specification (b) (4) % - (b) (4) %). Although, Phase I investigation did not reveal any assignable root cause, you proposed degradation of standard as probable root cause for lower area response (of the standard peak) that in turn caused higher assay result. You then retested the sample and based on the passing results invalidated the initial OOS results.

There was no justification as to why the standard degraded only in the standard of the initial test and not in the next standard preparation that was used in the hypothesis and in the retest of the sample. The implicated Batch No. (b) (4) was used to manufacture (b) (4) CAP USP (b) (4) MG-(b) (4) US) Batch No. (b) (4) Manufactured date 5/6/2020, Expiry date (b) (4) You shipped (b) (4) bottles (b) (4) capsules) to the US customers on (b) (4)

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OBSERVATION 2

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

Specially,

a. A review of the Sequence Audit trail data for Chromleon, revealed several examples where your analyst deleted samples and/or blanks from the sequence lists. Your procedure SOP_MDP_QC_013135 (5.0) Assigning User/System Policies and Management of Electronic Data in Chromeleon Network (Effective date 13 September 2022) has no provision of any kind of "Delete" operation from the Analyst. Some of the Sequence list with deleted sample and /or blanks included but not limited to: (b) (4) Suspension_Assay_310320_1-294, and (b) (4) (b) (4) Susp_Assay_310320_1-242. Many of your test methods do not contain sequence list, including but not limited to: (b) (4) USP (b) (4) mg/mL Specification No. FPF 1027R (04) Effective date 8/2/2022, and (b) (4) USP (b) (4) mg (b) (4) mL Specification No. FPF 122R (18) Effective date 10/4/2022.

b. On 11/14/2022, during walkthrough of your (b) (4) Room 2, Individuals were observed using a common password being used for the (b) (4) ID # (b) (4) 08. Your production manager stated that the password is shared amongst the operators. This (b) (4) does not store manufacturing data. This (b) (4) (ID # (b) (4) 08) is used for the manufacturing of (b) (4) Suspension. Some of the batches that shipped to the US market and are implicated with OOS results for (b) (4) uniformity assay, including but not limited to: OOS/C/20/MDP/FPDP/013 and OOS/C/20/MDP/SSDP/004.

c. Your General Manager of Quality provided a list of (b) (4) manufacturing equipment in the (b) (4) Formulation. Of the (b) (4) manufacturing equipment, 33 are on SCADA (21 CFR Part 11

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compliance), with the remaining manufacturing equipment that do not have data storage capability. The data that is created while product is manufactured on the equipment (that are not on SCADA) are not stored and /or cannot be recovered. Some of these equipment, include but not limited to: (b) (4) ID # (b) (4) -08, (b) (4) ID # (b) (4) -01), (b) (4) Filling Machine (ID # (b) (4) -02), and (b) (4) System (ID # (b) (4) -08).

OBSERVATION 3

Written procedures are not established for evaluations conducted at least annually to review records associated with a representative number of batches, whether approved or rejected.

Specifically,

Your Annual Product Quality Review for (b) (4) /SP (b) (4) mg (b) (4) mL and (b) (4) mg (b) (4) mL for February 2021 to January 2022 does not include (b) (4) batches that were manufactured in year 2021 including: (b) (4) Your General Manager of Quality stated that these batches were part of validation batches and were rejected in 2022. You also do not review (b) (4) uniformity data as part of the APQR. Your procedure SOP_MUM_CQA_010879(4.0) Annual Product Quality Review of Drug Product (Effective date 3/31/2022) is deficient such that it does not have provision for the review of (b) (4) uniformity data.

OBSERVATION 4

All records of production, control, distribution, components, and labelling associated with a batch of drug products were not maintained at least one (1) year after the expiration date.

Specifically,

On 11/14/2022 during walkthrough of your trash collection area, we observed 68 bags full of shredded documents. The Procedure and Control on Shredding of Documents, document number SOP MDP QA

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034114, dated 17 Sep 2021, establishes the process that is used to control the shredding of documents. The standard procedure is applicable, for example, for the following (Note: this is not intended to be an all-inclusive list), i.e., draft documents regarding specification/general test procedures, batch manufacturing records (BMR), proposals for change controls & supporting data, APQR meant for review purposes, Draft investigation report of OOS, OOT, Market complaints, deviations, incidents etc., document copy as Change Control, Deviation, Temporary Change Control, Complaint, CAPA used for reference to auditors/visitors as well as draft trend analysis reports of OOS, OOT, Complaint, deviation, Environmental monitoring, (b) (4) LIR, Change control etc. The above examples are placed inside "Drop Boxes". There are 30 Drop Boxes in Unit (b) and 15 Drop Boxes in Unit (b) (4). As an example, regarding draft documents related to marketed complaints, the Senior Executive-Quality Assurance and the Deputy General Manager-Quality Assurance confirmed that draft documents are used to prepare related marketed complaint reports. The draft documents / records are discarded and shredded. And the current logbooks that are used to document the specific documents that are shredded do not adequately describe or provide a detailed description of the GMP documents/records that are shredded.

On 11/21/2022, your Validation Manager from Quality Assurance shared an example of draft document that was placed in the Drop Box 18 on 11/12/2022. According to the Validation Manager, the document placed in the Drop Box 18 was a draft version of Performance Qualification Protocol of Checkweigher Due to Change in Pack Type of (b) (4) mL (b) (4) Suspension (b) (4) Document No. MDP16/PQP/CKW-07/22/004 Effective date 11/11/2022. Similarly, your Production Manager shared two documents (that were placed in Drop Box 09) including: Line Clearing Record of Manufacturing Area (b) (4) Annex_MP_QA_040308 (3.0) Batch No. (b) (4) and Batch Production Record Review Checklist Annex_MDP_QA_024647 for (b) (4) Capsule USP (b) (4) mg Batch No. (b) (4) Your Production Manager stated that these documents were empty however the respective drop box logbook could not verify either way.

OBSERVATION 5

Equipment used in the manufacture, processing, packing, or holding of a drug product lack appropriate design to facilitate operations for its intended use and for its cleaning and maintenance

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Specifically,

The Good Engineering Practices training module number MD2-TM-ENG2-FUN-001-00, dated 28/07/2021, is provided to all pertinent personnel that include the engineering department. The training includes for example, "Good engineering practices are to ensure that the development and/or manufacturing effort consistently generates deliverables that support the requirements for qualification or validation." The engineering drawings and specifications "define the level of accuracy required for engineering drawings, specifications…" and "define which document will be maintained as 'as built' records, how they will be maintained as accurate and checked on completion of the work." There are several concerns with regards to the current engineering practices e.g.,

a. There are (b) (4) individual HVAC Units that are used to provide HEPA filtered high quality air for the Formulation Manufacturing operations [i.e. (b) (4) form]. The Senior Manager of Engineering confirmed that there are no As Built diagrams/drawings for the (b) (4) HVAC units.

b. There are no As Built diagrams/drawings for the (b) (4) system that is used for the manufacture of (b) (4) forms.

c. There is an Isometric diagram (drawing number 100208002-02) dated 09/05/14 regarding the (b) (4) distribution loop. The Deputy General Manager of Quality Assurance explained that the personnel who prepared, checked, and approved the 2014 Isometric diagram no longer work at the company and confirmed that the engineering diagram has not been reviewed by the current QA department.

d. There is no Isometric diagram for the (b) (4) that is used for the (b) (4). The (b) (4) is used to provide (b) (4) to the clean the interior of the empty bottles for the (b) (4) forms.

e. The Senior Manager of Engineering confirmed that there is no document or standard operating procedure that defines or establishes good engineering practices.

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OBSERVATION 6

Routine calibration of automatic and mechanical equipment is not performed according to a written program design to assure proper performance.

Specifically,

The Metal Detection 2022 requalification protocol & report, document number MDP16/RQ/CFM-02/22-018 equipment tag number CFM-02 & MET-04, includes a challenge with (b) (4) (b) (4) challenge (b) (4) (approximately (b) (4) mm diameter). The Deputy General Manager of Quality Assurance confirmed that the requalification does not include a metal detection challenge with the (b) (4) standards inside the capsules (e.g., a size (b) (4) capsule is (b) (4) – (b) (4) mm and for a size (b) (4) capsule it is (b) (4) – (b) (4) mm closed joined length).

OBSERVATION 7

The responsibilities and procedures applicable to the quality control unit are not in writing and fully followed.

Specifically,

a. The Preparation, approval, issue and control of Drawing/Layout, document number SOP MDP QA 00492, dated 15 Jul 2020, defines & establishes the standard procedures regarding the engineering diagrams/drawings. Section 5.1.5.8 page 5, contains language with respect to the Quality Assurance person who approves the engineering drawing/layout. However, as confirmed by the Senior Executive Quality Assurance, the standard procedure is silent with respect to the content of the review and approval process.

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b. The Handling of Deviations, document number SOP MUM CQA 006948, dated 07 Jan 2021, established the process of handling of deviations in GMP operations. In section 5.41, page 10, the standard procedure describes "Deviation trends shall be prepared and evaluated (b) (4) by QA within (b) (4) of the (b) (4) end to determine if there are any trends developing which could be indicative." However, the standard procedure is silent with respect to the content of the trend evaluation process. A trend of the deviations is performed: however, the Executive Quality Assurance could not describe or explain the content of the trend evaluation that is performed.

OBSERVATION 8

The (b) (4) dosage forms are manufactured within Grade D (ISO 8) manufacturing areas / environment. During the (b) (4) HEPA filter integrity tests, there is a measurement taken to determine the particle levels within the Grade D areas under at-rest (static) conditions. However, there is no periodic particle measurements taken prior to, during or subsequent the manufacturing operations and as such there is no data to verify that the manufacturing areas are Grade D for the remaining (b) (4) manufacturing (b) (4)

API OBSERVATION

OBSERVATION 9

Investigations are inadequate to determine the root cause for the failure of a batch of intermediate or API to meet specifications whether or not the batch has been already distributed.

Specifically,

On 11/21/2022, your Investigation Manager reviewed OOS/C/20/MDP/FPDS/007 that was initiated to probe OOS result that was reported in related substances test by HPLC during analysis of (b) (4)

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USP Batch No. (b) (4) such that the observed result of any single unknown impurity was (b) (4) % against the specification limit NMT (b) (4) % (Finished Product Release Specification No. FPB 145-19, Effective date 10/6/2020). The Phase I investigation did not reveal any assignable root cause. Later you tested the Mobile Phase (b) (4) and found that the pH of mobile phase was (b) (4) against the specification of (b) (4) FPB 145-19, Effective date 10/6/2020). You then hypothesized the higher pH (b) (4) vs as the probable root cause and then retested the sample and based on the passing results, you invalidated the initial OOS results.

Review of the preparation record for Mobile Phase (b) (4) confirmed that the Mobile Phase (b) (4) (201009/APIFP/0909) was prepared at pH (b) (4) It is not clear at what time point the pH of the Mobile Phase (b) (4) changed from pH (b) (4) to pH (b) (4) e.g., during the initial analysis or after the analysis. You did not conduct the investigation of your manufacturing process to (at least) verify the critical process parameters. Review of your Maser Batch Record of (b) (4) USP suggested that the MBR did not have provisions to continuously monitor critical process parameters (including but not limited to temperatures). In most cases, (b) (4) emperature data is recorded for the duration of the critical process steps. The above implicated (b) (4) USP Batch No. (b) (4) was used in the manufacturing of (b) (4) CAP USP (b) (4) mg (b) (4) (US) Batch No (b) (4) Manufactured date 4/13/2021. Expiry date (b) (4) . You shipped (b) (4) bottles (b) (4) capsules) to the US customers on (b) (4)

OBSERVATION 10

Critical process parameters identified in the manufacture of APIs and API intermediates are not appropriately (continuously) monitored.

Specifically,

The equipment used in the manufacturing of your APIs and API intermediates is manually monitored for temperature during the particular stages of manufacturing by having the production operator read the temperature on DTI (digital temperature indicator) display and record in the batch record. Your

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MBRs (including but not limited to) for (b) (4) USP (Doc. No. 20000001078/32), (b) (4) USP (Doc. No. 20000001495/30), and (b) (4) USP (Doc. No. 20000001614/28) have provisions to record the start and end (b) (4) processing time and (b) (4) data of temperature for the duration of the (b) (4) processing operations. Similarly, you record (b) (4) temperature in the batch records for the (b) (4) stages. These findings in the MBRs were verified through the review of executed batch manufacturing records (BMRs) including but not limited to: (b) (4) Crude Intermediate, Material Code (b) (4) Batch No. (b) (4) (b) (4) Material Code (b) (4) Batch No. (b) (4) and (b) (4) Intermediate, Material Code (b) (4) Batch No. (b) (4) You do not have any alarm system to monitor the temperature probes which would identify if any temperature excursions occurred in critical manufacturing steps.

Your investigations to find the root cause into the manufacturing process to address any deviations, OOS results, and OOT are inadequate e.g., you lack manufacturing data that are related to critical process parameters (CPP).

OBSERVATION 11

Computer system do not have sufficient controls to prevent unauthorized access or changes to data.

Specially,

a. During review of the Sequence Audit trail data for Chromleon, I noted several examples where your analyst deleted samples and/or blanks from the sequence lists. Your procedure SOP_MDP_QC_013135 (5.0) Assigning User/System Policies and Management of Electronic Data in Chromeleon Network (Effective date 13 September 2022) has no provision of any kind of "Delete" operation from the Analyst. Some of the Sequence list with deleted sample and /or blanks included but not limited to: (b) (4) 310320_I-377, (b) (4) Residual Content_191220_I-244. Many of your test methods do not contain sequence list, including but not limited to: (b) (4) USP Specification No. FPB 339(12 Effective date 9/11/2021, and

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(b) (4) USP Specification No. FPB 101R (14) Effective date 7/7/2021.

b. Your General Manager of Quality provided a list of (b) (4) manufacturing equipment in the (b) (4) API manufacturing building. The list documents out of (b) (4) manufacturing equipment, 8 were on SCADA (21 CFR Part 11 compliance), but the rest of the manufacturing equipment did not have data storage capability. The data that is created while product is manufactured on the equipment (that are not on SCADA) are not stored and /or cannot be recovered. None of the (b) (4) were on SCADA and there is no data storage capability and hence no capability to continuously monitor the critical process parameters (CPPs). In (b) (4) API manufacturing building you manufacture APIs for the US market including: (b) (4) USP, (b) (4) USP, (b) (4) USP, (b) (4) USP, and (b) (4) USP.

Your General Manager of Quality provided a list of (b) (4) manufacturing equipment in the (b) (4) API manufacturing building. The list documents (b) (4) manufacturing equipment. 18 were on SCADA (21 CFR Part 11 compliance), with the remaining manufacturing equipment did not have data storage capability. The data that is created while product is manufactured on the equipment (that are not on SCADA) are not stored and /or cannot be recovered. In (b) (4) API manufacturing building you manufacture APIs for the US market including: (b) (4) USP and (b) (4) USP.

OBSERVATION 12

On 13/11/2021, a marketed complaint i.e., "Black Particle found in API powder during sampling" was received from a customer regarding (b) (4) USP batch number- (b) (4) CAPA number CAP-MA-001-22-0002, dated 14 Mar 2022 was initiated, which resulted with the installation of a (b) (4) for (b) (4) Room # (b) (4). The original equipment manufacturer (OEM) of the (b) (4) filter states "This is to certify that the filters supplied by us along with our (b) (4) is meeting the following specifications" that includes an efficiency of (b) (4) % down to (b) (4) micron and that the filter will "choked" between (b) (4) mm water column (we). However,

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov	11/14/2022-11/23/2022
	FEI NUMBER 3002807511
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mr. Rajendra B. Chunodkar, President Manufacturing Operations	
FIRM NAME Lupin Limited Unit I	STREET ADDRESS Unit 1, 198-202 New Industrial Area No. 2
CITY, STATE, ZIP CODE, COUNTRY Mandideep, Madhya Pradesh, India-462046	TYPE ESTABLISHMENT INSPECTED Pharmaceutical Manufacturer

a. The Operation, Cleaning of (b) (4) and Handling of Material Collected from (b) (4) document number SOP MDP MAM 019216, dated 06 Oct 2022, establishes to "check the differential pressure across the (b) (4) filter (It should less than (b) (4) mmwc)" and "If the differential pressure across the (b) (4) filter is found (b) (4) mmwe then rectify it before use". The standard procedure's "(b) (4) mmwc" is inconsistent with the OEM's specification of between (b) (4) - (b) (4) mmwc. (Note: the (b) (4) gauges on the (b) (4) are defined as a "Critical Process Control Instrument.")

b. The Batch Production Records (BPR) do not provide instructions to turn on the (b) (4) prior to, or during, the (b) (4) process. There is no record to document the actual mm of water column and to assure that the filter does not "choked" when the water column reaches (b) (4) mm.

c. The Corrective Action and Preventive Action (CAPA), document number SOP MUM CQA 016074, dated 31 Mar 2021, establishes the following i.e., "Target date of closure shall be displayed by-default considering (b) (4) from the date of initiation. However, target closure date can be modified (Less / more) from default date with appropriate justification in specific cases based on risk assessment of the issue and / or activity planner." Regarding the 13/11/21 marketed complaint the CAPA remains open i.e., to date that is 12 months.

d. Mindful of the concerns noted in the above observations there is no data to document that the CAPA is effective with respect to controlling the ingress of particles and to prevent the recurrence of the particles that are noted in the API marketed complaint.

OBSERVATION 13

The validation batch production records # (b) (4) dated 03/07/20, for the (b) (4) API Process Performance Qualification (PPQ) instruct for the (b) (4) process to "Load the (b) (4) material uniformly into the (b) (4) with the help of clean (b) (4) of approx. (b) kg capacity (b) (4) approx. (b) (4) in each (b) (4)". The General Manager of API Manufacturing confirmed that the (b) (4) (b) (4) mm (d) x (b) (4)

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NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Rajendra B. Chunodkar, President Manufacturing Operations

FIRM NAME	STREET ADDRESS
Lupin Limited Unit I	Unit 1, 198-202 New Industrial Area No. 2
CITY, STATE, ZIP CODE, COUNTRY Mandideep, Madhya Pradesh, India-462046	TYPE ESTABLISHMENT INSPECTED Pharmaceutical Manufacturer

mm (h)] does not provide any form of a measurable value (e.g., kg) and there is no record to document the volume or quantity of the (b) (4) material that is in the individual (b) (4) during the (b) (4) process.

OBSERVATION 14

The Good Engineering Practices training module number MD2-TM-ENG2-FUN-001-00, dated 28/07/2021, is provided to all pertinent personnel that include the engineering department. The training includes for example, "Good engineering practices are to ensure that the development and/or manufacturing effort consistently generates deliverables that support the requirements for qualification or validation." The engineering drawings and specifications "define the level of accuracy required for engineering drawings, specifications…" and "define which document will be maintained as 'as built' records, how they will be maintained as accurate and checked on completion of the work." There are several concerns with regards to the current engineering practices e.g.,

a. There are (b) (4) individual HVAC Units that are used to provide HEPA filtered high quality air for the Grade D (ISO 8) API (b) (4) manufacturing areas. The Senior Executive of Engineering confirmed that there are no updated As Built engineering diagrams/drawings for the (b) (4) HVAC units.

b. There are numerous pipes for the various manufacturing utilities and piping connections for the (b) (4) and vessels that are used for the manufacture of the API. The Manager Engineering confirmed there no Isometric diagrams for the numerous pipes that provide the various utilities and connections to the API (b) (4) and vessels used in the manufacturing processes.

c. The Manager of Engineering confirmed that there is no document or standard operating procedure that defines or establishes good engineering practices.

OBSERVTAION 15

The Preparation, approval, issue and control of Drawing/Layout, document number SOP MDP QA

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NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	FEI NUMBER 3002807511
Mr. Rajendra B. Chunodkar, President Manufacturing Operations	
FIRM NAME Lupin Limited Unit I	STREET ADDRESS Unit 1, 198-202 New Industrial Area No. 2
CITY, STATE, ZIP CODE, COUNTRY Mandideep, Madhya Pradesh, India-462046	TYPE ESTABLISHMENT INSPECTED Pharmaceutical Manufacturer

00492, dated 15 Jul 2020, defines & establishes the standard procedures regarding the engineering diagrams/drawings. Section 5.1.5.8 page 5, contains language with respect to the Quality Assurance person who approves the engineering drawing/layout. However, as confirmed by the Senior Executive Quality Assurance, the standard procedure is silent with respect to the content of the review and approval process.

OBSERVTAION 16

The (b) (4) API are manufactured within Grade D (ISO 8) manufacturing areas / environment. During the (b) (4) HEPA filter integrity tests, there is a measurement taken to determine the particle levels within the Grade D areas under at-rest (static) conditions. However, there is no periodic particle measurements taken prior to, during or subsequent the manufacturing operations and as such there is no data to verify that the manufacturing areas are Grade D for the remaining (b) (4) manufacturing (b) (4) (b) (4)

	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
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