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Prequalification Unit Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Finished Product Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**Lupin Ltd. (Jammu)**
Corporate address of manufacturer	Kalpataru Inspire 3rd Floor, off Western Express Highway Santacruz (East) Mumbai 400055, India
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Lupin (Jammu) EPIP, SIDCO Industrial Complex, Kartholi Bari Brahmana Jammu and Kashmir 181 133 India
Unit / block / workshop number	General products and Rifa products section
Inspection details	
Dates of inspection	9-12 July 2024
Type of inspection	For cause inspection
Introduction	
Brief description of the manufacturing activities	The Lupin Jammu site manufactures tablets, capsules, and metered-dose inhalers (MDIs) for both the domestic and export markets. All manufacturing activities are housed in one building block. A separate section within this block was dedicated to the manufacture of Rifa-FDC formulations. No beta-lactam products are manufactured at this site.
General information about the company and site	Lupin Limited was founded in 1968. The company is currently engaged in the manufacture of finished dosage formulations, APIs, and biotechnology-based products at various sites. According to the company's SMF and presentation, Lupin has 7 research centers spread across the USA, Mexico, Brazil, Netherlands, and India and 15 manufacturing facilities for both APIs and finished products, spread across India, the USA, Brazil and Mexico. The formulation facilities are situated at Verna (Goa), Pune, Aurangabad, Nagpur (Maharashtra), Mandideep, Indore, Jammu, Sikkim, Brazil, USA, and Mexico. The company's corporate office is located at Mumbai. The Jammu site is located on a 29609 square meter piece of land with a built-up area of 13900 square meters.

History	This was the fourth WHO-PQ inspection of the Lupin Jammu site. The site was previously inspected by WHO-PQT in November 2011, February 2014, and March 2018.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Documents reviewed included but were not limited to: • Quality Manual – management review meetings • Organization Chart • Job descriptions for key personnel • Personnel training and hygiene • Product Quality Review • Quality Risk Management • Responsibilities of the quality unit and production • Complaints and Recalls • Deviation handling and CAPA • Change control • OOS and OOT investigations • Material release • Self-inspection and vendor qualification • Validation and qualification • Equipment calibration • Data integrity • Sampling and testing of materials • Batch processing records • Materials management system • Analytical methods – stability • HVAC system • PW system Areas visited: • Starting materials, packaging materials, and FPP warehouses • Sampling and dispensing areas • Tablet manufacturing
Restrictions	Not Applicable
Out of scope	FPPs not submitted to WHO Prequalification were not included in the scope of this inspection.
WHO products covered by the inspection	Isoniazid/Rifampicin Tablet, Film-coated 75mg/150mg Ethambutol hydrochloride/Isoniazid/Pyrazinamide/Rifampicin Tablet, Film-coated 275mg/75mg/400mg/150mg Ethambutol hydrochloride Tablet, Film-coated 400mg Linezolid Tablet, Film-coated 600mg Isoniazid Tablet 300mg Moxifloxacin (hydrochloride) Tablet, Film-coated 400mg

Abbreviations	Meaning
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
APS	Aseptic process simulation
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
FEFO	First Expiry First Out
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GMP	Good manufacturing practices
GPT	Growth promotion test
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IQ	Installation qualification
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MFT	Media fill Test
MR	Management review
NC	Non conformity
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PW	Purified water
QA	Quality assurance

QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
RO	Reverse osmosis
SIP	Sterilization in place
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer
VMP	Validation Master Plan
WFI	Water for injection

Part 2	**Summary of the findings and comments**

1. Pharmaceutical quality system

The company had a well-documented pharmaceutical quality system, encompassing production, quality control and quality assurance activities at the site. A Quality Manual was in place and covered the essential GMP principles at the site. The manual referenced ISO 9001, ICH and various GMP guidelines. The quality manual generally described the expected elements of a pharmaceutical quality system including but not limited to, the company's organisational structure, document hierarchy, management of changes, deviations, complaints, product recalls, quality risk management, validations, and management review. A procedure for the preparation, review, approval, and control of corporate general documents, guided the establishment and review of the quality manual at the company. A training record for the quality manual and quality policy for company employees was available.

Management Review

Management review meetings were detailed in an SOP. The procedure described three levels of management meetings including: the quality council meeting (QCM) at corporate level conducted at a- minimum of six times per year, the site quality council meetings(monthly), and the global quality council steering committee meetings (quarterly).

The site Quality Head, was responsible for scheduling the site quality council meetings monthly as per the defined frequency, preparing and distributing the meeting agenda, documenting key decisions and action points, and following-up on actions and monitoring attendance of the site quality council meetings. Meetings were to be held by the 10th day of the following month. The composition and attendance of the quality council meetings were documented. Metrics to be discussed at each level were described in the SOP.

A separate procedure discussed the escalation of significant GMP events to corporate level. The procedure detailed the escalation of OOS results impacting commercial samples within one day, and for any other significant quality issues within two working days.

Site quality council meeting records for the months of May and June were selected for review. Minutes of the meetings were documented, and included action points, assignment of actions, and target completion dates. A review of the previous meeting minutes was performed.

Product Quality Review

A procedure for conducting product reviews was presented. The procedure was applicable to all drug products manufactured at all Lupin sites. PQRs were conducted on an annual basis. The QA department was responsible for performing product reviews based on data and information provided by the QA, QC, Production, and Regulatory Affairs departments. A plan for conducting PQRs was prepared within 30 days from the beginning of the year. PQRs had to be completed within 30 days from the target date. A 30-day extension could be granted upon justification. A statistical evaluation was carried out if more than 10 batches were manufactured during the review period. If fewer than 10 batches were manufactured during the year, then process capability was calculated, considering the batches manufactured during the previous year. If fewer than 10 batches were manufactured in 2 consecutive years, then CpK would not be calculated.

No batches of Rifampicin/Isoniazid tabs 150/75mg had been manufactured during the previous year. A PQR was conducted, including the relevant parts for review.

The APQR for Rifampin/Isoniazid/Pyrazinamide/Ethambutol 150/75/400/275mg tabs USP (1.09.2020 to 31.08.2021) was reviewed. 114 batches were manufactured during the review period. No batches were rejected, returned, or recalled.

The APQR for Rifampin/Isoniazid/Pyrazinamide/Ethambutol 150/75/400/275mg tabs USP (01.09.2022 to 31.08.2023) was also reviewed. No batches were manufactured during the review period.

The APQR report for Linezolid tablets 600mg, (01.11.2022 to 31.10.23) was reviewed. Products for different customers were assigned different product codes and these were included in the PQR. A total of 64 batches were manufactured in the period of review. The following changes related to the APQR were also reviewed:

- Change control validation of blister forming temperature at 100-140^{0}C. This was conducted as an addendum to the process validation as it was not previously considered, a notification was sent to WHO and this was approved. A risk assessment was performed as part of the change.
- Change control water determination test limit to NMT 0.50% from 0.5% and skip testing for residual solvents and impurities. Initiated 10th April 2023, categorized as major, notification sent to WHO. Specifications were revised on the 17th April 2023. A risk assessment for skip testing residual solvents and impurities for the linezolid API, initiated on 13.04.203, was conducted using the FMEA tool. A cross-functional team of QA and QC was involved. WHO was notified of the risk assessment.

Quality risk management (QRM)

A systematic process for the assessment, control, communication, and review of risks related to GMP activities and the products manufactured on-site was followed by using quality risk management. Risk management was applied both prospectively and retrospectively and a procedure was in place describing the steps to be followed. QRM was integrated into the QMS, and examples of risk assessments for changes, deviations, and manufacturing processes were reviewed.

Deviations

Deviations were handled according to a written procedure. This was a corporate procedure. Deviations were electronically registered within one working day from reporting. The person in charge of a group (initiator) had access to the electronic system and was responsible for registering the deviation. The name of the person identifying the deviation and the person registering the deviation were recorded on the deviation report. Recurrence of the deviation in the last 24 months had to be checked and if confirmed, had to be referenced in the new deviation report. The initiator had to conduct a preliminary investigation and, with the assistance of the QA department, perform an initial impact assessment to determine immediate actions and corrections. A matrix was used to initially assign criticality (critical, major, or minor). The deviation could be re-classified based on further investigations and identification of the root-cause. The deviations classified as critical were prioritized and had to be closed out within 15 working days, while all other deviations had to be closed out within 30 days. Up to two 30-day extensions could be granted upon justification. Instructions on handling deviations in case the electronic system was out of order were in place. Upon determination of the root-cause, CAPA were identified and their implementation was monitored. Trending of deviations was performed quarterly.

Antimicrobial Resistance

The company manufactured several antibiotic containing finished products, and the issues of AMR and waste management were discussed. According to the company, when a new product was introduced at the facility, among the information that had to be evaluated was Environmental Health and Safety related components including data on starting material, intermediates, auxiliary materials, solvents, and finished products. This information was mostly provided in the form of MSDS. Additionally, waste cards were established, providing the source and approximate quantity of liquid, solid, and gaseous emissions from the process, washings, and infrastructure facilities (e.g., boiler). Furthermore, data on proposed treatment methods of liquid, solid and gaseous wastes and special requirements regarding storage and disposal were included as part of a checklist. Finally, a risk assessment had to be performed including, mostly occupational and process risks. Lupin had established a contract with a service provider for the collection, transport, treatment, and disposal of hazardous waste. An Effluent Treatment Plant was also established and a procedure for its operation was in place. Collection and disposal of waste and rejected material from production was governed by the rules described in a written procedure. The company occasionally checked the levels of antibiotics in ETP water (sludge, inlet, outlet). Test reports for Ethambutol and Levofloxacin were presented. The residues of Ethambutol were below the limit of detection in the outlet water. It was noted that some levofloxacin concentration was identified in the ETP outlet water. According to the company this concentration was acceptable by the local authorities.

The information and checklists for the introduction of the products Levofloxacin, Linezolid, and the combination product Rifampicin/Isoniazid/Ethambutol/Pyrazinamide were presented. The levels of Linezolid, Rifampicin, Isoniazid, and Pyrazinamide in ETP output water had not been checked by the time this inspection took place. The company committed to periodically test the antibiotic level in ETP output water.

All the observations identified regarding the QMS during the inspection were adequately addressed by the manufacturer.

2. Good manufacturing practices for pharmaceutical products

Good manufacturing practices were generally implemented. Manufacturing processes were clearly defined in SOPs and systematically reviewed. Necessary human and physical resources, including adequate premises, equipment, and utilities, were provided for the current manufacturing activities. Qualifications/ validations, calibrations and maintenance were performed according to the VMP and prepared protocols and followed the relevant established procedures. The manufacturing processes followed procedures as defined and documented in the BMRs. The personnel were appropriately qualified.

All the observations identified during the inspection were adequately addressed by the manufacturer.

3. Sanitation and hygiene

Documented procedures were in place detailing sanitation and hygiene principles at the company. Change rooms were appropriate and equipped with adequate gowning facilities and hand sanitization stations. Employees accessing core manufacturing areas were required to appropriately gown prior to entry. A pre-employment and periodic medical examination was implemented for both permanent and contract personnel and this was well documented. The sanitization and hygiene measures in place at the time of inspection were found to be acceptable.

All the observations identified during the inspection were adequately addressed by the manufacturer.

4. Qualification and validation

The VMP described the principles and requirements for qualification/validation of critical equipment, utilities, facilities, processes, instrumentation, cleaning, personnel, and computerized systems. It was reviewed every two years. A guidance programme was included in the VMP and maintained in the form of an Excel spreadsheet to monitor the validation activities and ensure they were completed within the established target dates.

HVAC

A procedure for conducting performance validation/verification of the HVAC system was presented. It provided appropriate instructions for establishing qualification/verification protocols.

The protocol for performance validation/verification of the HVAC system was made available. The protocol included all the AHUs on-site. The qualification of the AHU providing filtered air to the Rifa dispensary was reviewed. The tests, frequency and acceptance criteria were appropriately defined. For the non-viable particle count, the minimum number of sampling locations was determined based on ISO 14644-1:2015.

The validation summary sheet for the Rifa dispensary (Dispensing Booth 3) was reviewed in detail. The qualification was contracted out to a third party. Certificates for standard instrumentation used during qualification were presented except for the measurements relating to temperature, relative humidity, and differential pressure where the already installed instrumentation was used.

Cleaning Validation

A procedure defining the requirements for cleaning validation was presented. The procedure was applicable to cleaning procedures for all equipment and process aids coming in direct contact with the product. The cleaning validation process used a bracketing approach considering the product (API/strength/potency/composition), the process, the type of equipment, and the batch size to identify the worst-case scenario. The cleaning validation process included the following stages:

1. Development of the Cleaning Validation Protocol/ evaluation of equipment surfaces/ identification of worst-case product.
2. Determination of acceptance criteria.
3. Analytical method development.
4. Determination of the most suitable method of cleaning for the equipment train.
5. Execution of 3 cleaning validation runs.
6. Generation of the cleaning validation report.

Instructions on the use of swabs and rinse samples were provided. A procedure for the determination of Acceptable Daily Exposure (ADE) was in place.

Equipment Qualification

The qualification of equipment, systems and facilities for the manufacturing/packaging of drug products was described in a written procedure. The SOP described the key elements of equipment qualification such as DQ IQ, OQ, and PQ. URS was required for each equipment prior to procurement. Periodic requalification was to be performed every three years for critical equipment and every 5 years for less critical equipment. However, this period could be shortened based on risk assessments and breakdown records of the equipment.

All the observations identified regarding qualification/validation during the inspection were adequately addressed by the manufacturer.

5. Complaints

A corporate procedure for handling complaints was in place. The procedure provided instructions on receiving, registering, investigating, applying CAPA, communicating with the customer and closing out a complaint. Complaints were registered and handled in an electronic system. Complaints were categorized as critical, major, minor, adverse drug events, lack of effect, medical information, and drug-device handling issues. Based on the impact on quality, efficacy, and safety, the investigation was prioritized accordingly. Complaints had to be closed out within 30 days. Up to two extensions could be granted if justified, and a risk assessment had to be carried out in support of the extension. Trending of complaints was carried out quarterly and annually.

WHO Prequalification was informed by the Stop TB Foundation on 29.04.2024 of several quality defects affecting two batches of Linezolid 600mg tabs. The information on this complaint was further investigated during the inspection.

All the observations identified during the inspection were adequately addressed by the manufacturer.

6. Product recalls

There was a corporate procedure in place for the timely withdrawal of defective products/batches from the market. The decision for recall was taken by the Head of QA, the Site Quality Head, and the Head of Corporate QA. Recalls were classified as voluntary or statutory, and depending on the risk to patient health, they were categorized as Class I, II, or III. The depth of recall was defined (consumer/user level, retail level, wholesale level) in the SOP. A mock recall had to be conducted once per year according to a defined protocol unless a recall had taken place during the year.

All the observations identified during the inspection were adequately addressed by the manufacturer.

7. Contract production, analysis, and other activities

The residual solvent testing for Linezolid tablets/drug substance by GC was contracted out to two external laboratories. The SOP for the qualification of contract testing laboratories was reviewed.

All the observations identified during the inspection were adequately addressed by the manufacturer.

8. Self-inspection, quality audits and suppliers' audits and approval

Qualification of vendors was detailed in an SOP. The procedure described the selection, evaluation, approval, and periodic assessment of manufacturers of raw materials. Vendor qualification was initiated by the corporate global supply division. The approval process involved a site audit, evaluation of documentation, and quality control of raw material samples. A matrix for vendor approval detailed the documents that were required to be submitted during the approval process for a vendor. The documents were applicable to both new and existing material vendors. Examples of vendor qualification including, the relevant audit reports, were reviewed.

All the observations identified during the inspection were adequately addressed by the manufacturer.

9. Personnel

Lupin had an adequate number of personnel with the necessary qualifications and practical experience. Responsibilities of staff and their specific duties were detailed in written job descriptions. Personnel interviewed during the inspection were aware of the principles of GMP in general.

The site organogram was presented and followed the format described in the written procedure for job responsibilities. The organogram reflected independent reporting lines for key personnel at the site. Production reported to the site Head, whereas the Quality Assurance, and Quality Control functions were separate and reported to the Head of Quality. A template was used for documenting job descriptions (JD). The job descriptions of the QA manager, QC manager, and Lab QA reviewers were checked. The JDs were generally comprehensive and signed by the individual job holders. The reviewed JDs included the role description, key deliverables, and delegation of duties in cases of absence.

All the observations identified during the inspection were adequately addressed by the manufacturer.

10. Training

Training activities were described in the training procedure. The scope of the procedure covered both permanent and contract workers. The site training coordinator was responsible for managing training in consultation with user departments. Training needs were identified by department heads for individuals based on the nature of their work, audit observations, deviations, complaints etc. Training were categorized as induction, ongoing, functional, and remedial training. Annual training schedules were prepared department-wise. The training schedule for the year 2024 included dates, topics, target group, actual training date, name of instructor, and signature. Training records were managed in the Learning Management System. Staff who were away from their duty stations for over 90 days had to be re-trained before resuming work.

The training records for consolidated GMP topics conducted in March were verified in the Learning Management System. The training record comprised the number of target and actual attendees, learner name and, score. Internal trainers were certified based on experience and qualification. A list of qualified internal trainers was available.

A separate software was used to manage the training for contract workers. A similar system was maintained as that for permanent workers.

All the observations identified during the inspection were adequately addressed by the manufacturer.

11. Personal hygiene

Personnel hygiene was described in a written procedure. Employees were trained on basic hygiene practices related to GMP. Operators were required to wear protective garments prior to accessing core manufacturing areas. Entry and Exit procedures into clean rooms were well displayed in change rooms. The Health Checkup Procedure described the induction and periodic medical examinations for all employees working in core areas. Employees affected by viral and infectious diseases were required to inform their supervisors and were excluded from working in core areas.

All the observations identified during the inspection were adequately addressed by the manufacturer.

12. Premises

The buildings on-site covered an area of approximately 13900m^2. In general, the premises had adequate space for the orderly placement of equipment and materials. The flow of material and personnel was designed to prevent contamination and mix-up. Layouts of the facilities were provided. Separate raw, packing material and finished goods warehouses were available. Temperature and relative humidity were monitored and controlled. Dedicated storage areas for empty capsules and temperature-sensitive materials (2-8ºC) were available. There were three dispensing rooms, which were also used as sampling rooms. One of these dispensing rooms was dedicated to Rifa products. The core manufacturing area was located on the ground floor and designed to manufacture oral dosage forms (OSD). It was divided into Rifa and non-Rifa products. A separate area was dedicated to metered dose inhalers (MDI). The HVAC system consisted of several AHUs. The entire manufacturing area was provided with terminal 0.3µm HEPA filters except for the packing hall (secondary packaging- 0.5µm filters). In general, the process corridors had higher pressure than the individual rooms to prevent any ingress of air/powder from the room to the corridor. Laboratories were located on the first floor.

All the observations identified during the inspection were adequately addressed by the manufacturer.

13. Equipment

In general, production equipment was of appropriate standard and records of preventive maintenance were kept. The equipment appeared to be installed to facilitate production and reduce the risk of contamination and mix-ups. All production equipment reviewed was identified as to its content or purpose with cleanliness status identified by appropriate labels. Cleaning records were presented. Cleaning and use were recorded electronically on an electronic system. To produce non-Rifa products, two granulation, two mixing and two compression machine rooms were available. Procedures for the setup and operation of production equipment were made available.

All the observations identified during the inspection were adequately addressed by the manufacturer.

14. Materials

Written procedures for the receipt, identification, quarantine, storage, handling, sampling, approval, or rejection of materials were in place. Material receipt operations included several controls to verify the transport conditions, the origin, identity and quality of the material and the containers. A checklist was used to document these controls. Upon completion of the receipt activities, the material information was entered into SAP and the material labels were printed out. SAP was used to manage the status and inventory of the raw and packaging materials. FEFO principles were incorporated into the system and were checked during the inspection. Instructions were in place for handling damaged containers. Temperature and relative humidity were controlled and monitored. There were three sampling/dispensing rooms. FPPs were received at the warehouse according to the instructions described in a written procedure. Finished products for export were assigned unique track and trace labels which were affixed to each carton. Cartons of finished products for the domestic market were wrapped on a pallet, and a single barcode label was affixed to the pallet load.

All the observations identified during the inspection were adequately addressed by the manufacturer.

15. Documentation

A procedure for the preparation, review, approval, and control of SOPs was established. The SOPs were managed by an Electronic Documentation Management System. There were instructions on the introduction of new site-specific and corporate procedures. For a new SOP, a 45-day window was given after approval for the SOP to become effective. During this timeframe, training for concerned personnel had to be performed.

A procedure for the storage, retrieval and destruction of quality related documents and records was presented. The storage facilities and measures in place to protect quality documents were defined. Records or data stored in electronic form were retained according to a written procedure. Retention times were defined.

The SOP on Master Data maintenance in SAP was discussed. The purpose of the procedure was to define guidelines for the creation of the master data in all SAP modules. More specifically, there were instructions in place for establishing and maintaining master data in the following modules: material management, production planning, quality management, sales and distribution, plant maintenance, warehouse management system and financial accounting and controlling.

There was a procedure in place describing the generation and allocation of batch numbers. This was a corporate procedure applying to drug substances, intermediates, by-products, recovered solvents, semi-finished products, finished products, reprocessed/ reworked batches, blended, and exhibit batches. The batch number would be automatically generated in SAP at the time an order was created.

All the observations identified during the inspection were adequately addressed by the manufacturer.

16. Good practices in production

In general, there were procedures in place providing appropriate instructions for the activities, operations and processes taking place in the manufacturing areas. Dispensing activities followed the principles described in an SOP. The use and cleaning of the dispensary were registered electronically in the e-Log. Filter bags used in FBDs were product dedicated, were uniquely identified and their integrity was checked before and after use and documented in the batch record. Manufacturing and packaging batch records were maintained and completed contemporaneously. Spot checks on batch records and line clearance were performed during the tour of the facilities.

All the observations identified during the inspection were adequately addressed by the manufacturer.

17. Good practices in quality control

The Quality control laboratories were located on the first floor and were separated from the production areas and tasked with the physical, chemical, instrumental, and microbiological analysis of starting, and packaging materials, bulk-finished products, as well as FPPs. The QC laboratory was appropriately organized and equipped. Analytical equipment was installed in separate rooms. The Quality Control department was responsible for performing sampling on raw and packaging. 100% sampling for ID testing was applied to APIs and excipients and a composite sample was used for full testing except for APIs manufactured by Lupin sites where 100% ID testing was performed but full testing was performed in one batch per year. Sampling of packaging materials followed the principles described in a written procedure. Raw material and FPP samples were received at the laboratory, and their allocation was registered on a spreadsheet. A sample registration was used for tracking the quantities used for testing and a final reconciliation was performed. There were procedures in place providing instructions for the preparation of reagents, volumetric solutions, and samples to be tested. The inventory of reference and working standards was managed in SAP. Working standards vials were single-use. Records for the preparation and analytical worksheets were maintained.

Stability studies.

Lupin maintained separate sections that housed the stability chambers, on the first floor adjacent to the quality control laboratory.

Five stability chambers including a standby chamber, were available to support the conduct of stability studies at all climatic zone conditions. Access to the stability areas was restricted to authorised personnel and controlled through electronic card access. Chamber storage conditions were continuously monitored online, and alarms were triggered in case of excursions. The temperature and relative humidity records for the chambers were reviewed. No alarms requiring action were noted.

The conduct of stability studies was adequately detailed in the relevant procedure.

Retention samples

Retention samples were kept in a lockable room with restricted access on mobile racks on the same floor as the stability chamber room. Locations of samples were tracked in the SAP. Storage conditions in the retention sample area, were periodically monitored against established limits. Retention sample storage was managed in accordance with a written procedure. An annual inspection of samples was performed to assess physical quality attributes.

Out of Specification
The procedure for handling OOS results was presented. Investigations were divided into different phases. Phase I investigations focused on identifying laboratory errors and hypothesis testing was performed if a probable cause was identified. Phase II investigations were extended to production and process development.

Microbiological laboratory
The laboratory was located on the first floor of the main building. It was an extension of the instrumentation laboratory. The laboratory was visited on the last day of the inspection. Access was restricted to authorized personnel, and a change room was available before entry. The main room housed the 5 incubators. A procedure was in place for carrying out microbial contamination test, and it followed the principles described in USP. For products having antimicrobial activity a neutralization/pretreatment step was applied using 0.5% Soya Lecithin and 4% Polysorbate 20 in a 1:10 ratio with the sample.

Purified Water
There were 23 user points on the PW loop and two extra sampling points (distribution tank and return loop). A procedure for testing PW was established. The 23 user points were sampled once per month, while the distribution tank and return loop sampling points were sampled daily. Conductivity, TOC, Acidity/Alkalinity, Heavy metals, nitrates, oxidizable substances, TAMC, and specified organisms were performed. TAMC, TOC, and Conductivity values were trended (return loop sampling point). Alert and action limits were established. The monitoring reports for May 2024 for the distribution and return loop sampling points were presented.

All the observations identified during the inspection were adequately addressed by the manufacturer.

Part 3	**Conclusion – Inspection outcome**

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, of ***Lupin Ltd Jammu***, located at ***EPIP, SIDCO Industrial Complex, Bari Brahmana, Jammu (J&K)-181133 India*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines.

All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the WHOPIR, were addressed by the manufacturer, to a satisfactory level, prior to the publication of the WHOPIR

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

Part 4	List of WHO Guidelines referenced in the inspection report

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2.
   Short name: WHO TRS No. 986, Annex 2
   https://www.who.int/publications/m/item/trs986-annex2

2. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2.
   Short name: WHO TRS No. 957, Annex 2
   https://www.who.int/publications/m/item/annex-2-trs-957

3. WHO guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report. Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 9.
   Short name: WHO TRS 1010, Annex 9
   https://www.who.int/publications/m/item/trs1010-annex9

4. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3.
   Short name: WHO TRS No. 1033, Annex 3
   https://www.who.int/publications/m/item/annex-3-trs-1033

5. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4.
   Short name: WHO TRS No. 929, Annex 4
   https://www.who.int/publications/m/item/annex-4-trs-929

6. WHO good practices for pharmaceutical quality control laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-seventh Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052), Annex 4.
   Short name: WHO TRS No. 1052, Annex 4
   https://www.who.int/publications/i/item/9789240091030

7. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3.
   Short name: WHO TRS No. 957, Annex 3
   https://www.who.int/publications/m/item/trs957-annex3

8. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8.
   Short name: WHO TRS No. 1010, Annex 8
   https://www.who.int/publications/m/item/Annex-8-trs-1010

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