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Prequalification Team Inspection Services
WHO PUBLIC INSPECTION REPORT
Active Pharmaceutical Ingredients

Part 1	**General information**
Manufacturers details	
Name of manufacturer	Olon Active Pharmaceutical Ingredients India Private Limited
Corporate address of manufacturer	Olon Active Pharmaceutical Ingredients India Private Limited Unit No. 3B-38, 39 and 40, 3rd floor, Phoenix Paragon Plazza, Phoenix Market City, L.B.S. Marg, Kurla (W), Mumbai-400070 India. Tel. No.: + 91 022 6834 0000
Contact person:	Mr. Manik Garje Head Quality, manik.garje@olonindia.com
Name & address of inspected manufacturing site if different from that given above	Olon Active Pharmaceutical Ingredients India Private Limited Plot Nos. L-1, L-21 to L-28 & L-44 Additional Phase MIDC, Mahad, Raigad Dist, Maharashtra -India Pin Code: 402301 GPS address: Latitude: 18°6'17" N Longitude: 73° 30' 59" E. D-U-N-S: No: 91 – 862 – 9309

Plants and buildings	• Rifampicin plant
	  ○ Rifampicin Fermentation building No 12
	  ○ Rifampicin Synthesis building No 8
	• Solvent recovery plant, building No 9

Inspection details	
Dates of inspection	14 – 17 October 2019
Type of inspection	Routine
Introduction	
Brief description of the manufacturing activities	Manufacture, quality control and release of non-sterile products - Bulk Active Pharmaceutical Ingredients and saleable Intermediates
General information about the company and site	API manufacturing site is located 180 Km South of Mumbai (on Mumbai Goa Highway) in the city of Mahad, Raigad District, India (Latitude: 18° 6' 17" N, Longitude: 73° 30' 59" E). Formerly Sandoz Private Limited, India, is a fully owned company of Sandoz AG, the generic drug division of Novartis Group, global pharmaceutical company headquartered in Basie, Switzerland. The Indian operations were set up in 1997 as a joint venture under the name Ciba CKD Biochem Ltd. to produce Rifampicin. This operation was merged with Novartis in 2001 and changed to the Sandoz API - Business Unit in 2005, as

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	part of internal reorganization of Novartis when Sandoz AG was created. In 2007, the Sandoz Mahad site registered with the U.S. FDA as a producer of API's from additional API Plant (MSP Plant). In 2018, the Novartis divested Mahad facility to Olon S.p.A Italy. Ownership is changed from Sandoz Private limited Mahad to Olon Active Pharmaceutical Ingredients India Private Limited with effect from 1 April 2019. At the site the company has two manufacturing plant for Active Pharmaceutical Ingredients (API-Bulk Drugs). One plant (hereafter termed as Rifampicin plant) is a dedicated facility used for manufacturing of Rifampicin (API) and Rifamycin O Pure (Intermediate) only. The second API Plant is a multi-synthesis facility used for manufacturing of APIs. MS&T Laboratory has been established at site to support the continuous improvement in the manufacturing process to manufacture the cost competitive product. Kilo lab is completely dedicated for manufacturing of development batches. The site operates three 8-hour shifts (24/7) *One OLON* Olon is an Italian company world leader in the Active Pharmaceutical Ingredients (APIs) production, using synthetic and biological processes for Generic market as well as in Contract Development and Manufacturing (CDMO). OLON Headquarter is situated at Rodano (Milan, Italy), Olon has 10 manufacturing facilities – 7 located in Northern Italy, 1 in Spain and 1 in USA, 1 in India. 3 branch offices: Hamburg (D), Floram Park NJ (USA) and Shanghai (China). All manufacturing sites are regularly inspected by the national and international Health Authorities, and regularly audited by our partners and customers.

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History	

Authority	Date/s of inspection
Maharashtra State FDA	19th - 20th Nov 2014
TGA Australia	1st - 5th Dec 2014
USFDA	1st - 5th Dec 2014
CDSCO	04th - 5th Aug 2015
Maharashtra State FDA	17th Dec 2015
ANVISA	17th - 21st Oct. 2016
Maharashtra State FDA	26th March 2017
Maharashtra State FDA	11th July 2017
CDSCO	11th - 12th Oct 2017
TGA Australia	5th - 8th Dec 2017
Maharashtra State FDA	12th Jan 2018
Joint Inspection CDSCO and Maharashtra State FDA	25th March 2019
Joint Inspection CDSCO and Maharashtra State FDA	11th - 3th June 2019

Areas inspected	Please see Part 2
Restrictions	APIs out of PQ
Out of scope	Parts of the site not concerned with the manufacture of the above API and intermediate were not inspected.
WHO products numbers related to this the inspection	• Rifampicin non-compacted • Rifampicin compacted • Rifampicin micronized • Rifampicin milled
Abbreviations	**Meaning**
ADE	Acceptable daily exposure
ADR	Adverse drug reaction
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APQR	Annual product quality review
AQL	Acceptance quality limit
BMR	Batch manufacturing record
BPR	Batch production record
CAPA	Corrective and preventive action
CC	Change control
CCEA	Complete, consistent, enduring, available
CFU	Colony-forming unit

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CIP	Cleaning in place
CoA	Certificate of analysis
Cpk	Process capability index
DQ	Design qualification
EDI	Electronic deionization
EHS	Environment, health and safety
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FTA	Fault tree analysis
GMP	Good manufacturing practices
GPT	Growth promotion test
HACCP	Hazard analysis critical control point
HAZOP	Hazard and operability study
HEPA	High efficiency particulate air
HPLC	High-performance liquid chromatography (or high-performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
ICH	International Council for Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IQ	Installation qualification
KPI	Key performance indicators
LAF	Laminar air flow
LIMS	Laboratory information management system
LOD	Limit of detection
LOQ	Limit of quantification
MACO	Maximum allowable carry over
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MR	Management review
NC	Non-conformity
NCA	National control authority
NCL	National control laboratory
NRA	National regulatory agency
OMCL	Official Medicines Control Laboratory
OOS	Out of specification
OOT	Out of trend
OQ	Operational qualification
PDE	Permitted daily exposure
PHA	Process hazard analysis
PLC	Programmable logic controller
PM	Preventive maintenance

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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
RH	Relative humidity
RO	Reverse osmosis
RPN	Risk priority number
SMF	Site master file
SOP	Standard operating procedure
UPS	Uninterrupted power supply
URS	User requirements specifications
USP	United States Pharmacopoeia
UV	Ultraviolet-visible spectrophotometer
WS	Working standard

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

1. Quality system

Principle

Production and control operations were specified in written form and GMP requirements were essentially being met. Managerial responsibilities were specified in written job descriptions. Product and processes were monitored, and the results were reviewed as part of the approval process of batch release. Regular monitoring and reviews of the quality of pharmaceutical products were being conducted according to specified procedure.

Data integrity

The following SOPs related to the data integrity were checked:

- "Data Lifecycle Pathway Mapping". SOP Described procedure for the assessment of data pathway for a process - all phases in the life of the data (including raw data) from creation, processing, review, reporting and retention,
- "GxP Computerized System (CS) Compliance". SOP described validation approach of systems software and the qualification activities associated with the computerized systems. System lifecycle management - user management, data backup, restoration and audit trial review.
- "Access Control & User Management"

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- "Procedural control and the Audit Trails review of Laboratory Equipment / Instrument". Audit trail review was conducted as part of the batch review, prior to approval and release of the analytical data. Batch wise audit trail review was performed by QC reviewer according to the Check
- "GxP Electronic Data Review". SOP described key requirements for review of GxP relevant electronic data, produced/captured, processed and stored computerized system to ensure the integrity of critical data at system level
- "Validation and Usage of Microsoft excel Spreadsheets". According to the SOP all spreadsheets used in calculation of analytical results should be validated and version controlled. Excel sheets were used for the calculations which were not in Chromeleon system
- "User management in Chromeleon Chromatography networking system",
- "Integration of chromatographic peaks". Manual integration (MI) was allowed for related substances and residual solvents tests.

Management review (MR)
SOP "Quality Management System" and last MR meeting minutes were checked. Meetings were held monthly. Quality committee had 4 core members.Standard agenda (minimum) was specified. Meeting minutes and presentations discussed during the last meeting were presented to inspector.

Product Quality Review (PQR)
SOP "Annual product review" and plan for preparation of APQR were checked. APQR was carried out according to the rolling schedule and should be completed within 3 months. Minitab was used to calculate Ppk, statistical process control charts also were use. Ppk target level was NLT 1.33.

PQR for time period 01-05-18 to 30-04-19 was checked. One PQR was prepared for all different grades.

Ongoing process verification
Part of the PQR was Annually ongoing process verification (OPV) report, what was checked. OPV procedure was explained in the "Annual product review". SOP explained ongoing (continued) process verification or stage 3 of process validation.

Quality metrics and key performance indicator (KPI)
SOP "Quality metrics and key performance indicator (KPI)" was checked. SOP was applicable for all departments and defined minimum requirements for monitoring, evaluation and review of the KPIs as well as monthly quality metrics performance reporting. Quality metrics & KPI monthly reports for July, August and September and Annual Quality system review: Mahad 2019 were checked.

Documentation and records
SOP "Good Documentation Practices". SOP included real examples (photo copies) how any alterations etc. should be made and documented.

SOP "Printing of labels" was checked. SOP describes handling of quarantine and release labels in the starting materials warehouse.

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Self-inspection

SOP "Quality Audits, inspections and Auditor Certification" was checked. SOP described initial certification of GxP auditors and auditor's certification as well as self-inspection process and post inspection activities. List of certified auditors were presented. According to the SOP planned self-inspection was performed for all departments quarterly according to the department wise check lists. QC self-inspection report from 22-08-19 was checked.

Quality Risk Management (QRM)

Assessment report for data life cycle pathway mapping "Standalone computerized systems – FTIR" was checked.

SOP "Quality risk assessment" was Checked. The quality assessment was performed when a new product was manufactured or in case of major changes, but it was not performed periodically.

Deviations

SOP "Handling deviations", its flow chart and registers were checked. Deviations were recorded to BMRs/BPRs and analytical work sheets. Classification of deviations were as:

- Critical
- Major
- Minor

According to the SOP deviations should be closed within 30 calendar days, if not possible one extension was allowed and should be approved by QA. SOP explained root cause analysis. Deviations were trended quarterly. Several deviation forms and related CAPA forms were checked.

Corrective actions and preventive actions (CAPA)

SOP "Action & corrective and preventive action (CAPA) management", its flow chart and registers were checked. SOP was applicable to deviations, OOS/OOE, lab incidents, complaints and inspections/audits.

Change control (CC)

SOP "Change control management" its flow chart, registers and change matrix were checked. SOP was applicable to GxP and non GxP changes. Several CC were checked.

Complaints

SOP "Technical complaint handling", its flow chart and register were checked. Complaints were classified as:

- Technical complaints:
    - Critical
    - Major
    - Minor

Complaints were received by marketing department and send to the site QA. All complaints should be investigated and closed within 30 days, if not possible extension should be granted by QA. A

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number of complaint investigation records was checked

Recalls

SOP "Product recall" was checked. The company stated that till inspection there were no recalls. SOP classified class I, II and III recalls. Recall effectiveness was evaluated by mock recall, preformed every 3 years.

Personnel

Department	**Employees at Site Mahad –India**
V.I. Production	70
Rifa Production	59
Quality	47
Engineering	38
MS&T	14
SCM (Planning, Warehouse, Direct Purchase)	10
HSE	08
Finance & Legal	01
HR, Training, Site Administration	04
Information Technology	01
Regulatory	01
Site Management	01
Total	254

Training

SOP "Training, Qualification and Certification of personnel". All associates joining the company must undergo on-boarding training (including Data Integrity, Good Documentation Practices, Basic cGMP etc.)

SOP "Personnel qualification" and its flow chart were checked. SOP was applicable to QC/IPC/AS & T analysts working in GxP area. Analysis qualification was performed by given previously analyzed sample or alternatively the analysis can be performed simultaneously with the current testing by an experienced analyst. Personnel qualification records for Ms. XX for HPLC related substances Mr. ZZ for Foreign growth management in the fermentation process test were checked.

2. Production system

Production operations followed defined procedures. Significant deviations from the initial protocol were recorded and investigated, root causes were determined and CAPAs were implemented where necessary. Checks on yields and reconciliation of quantities were carried out. Access to production premises was restricted to authorized personnel.

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Production process / Plant tour

Dedicated Rifampicin plant was used for manufacturing of Rifampicin (API) and Rifamycin 0 Pure (Intermediate) only. This plant consisted of two production buildings: fermentation and synthesis. During the inspection, fermentation process was going on. Synthesis was only done for the intermediate Rifamycin O. This was isolated from the process and sold to the market as starting material for different API.

Full process of Rifampicin production was explained in detail. Product flow was followed and relevant equipment, dedicated for this process was seen.

Batch Production Record (BPR)

Batch manufacturing record of Rifampicin Batch No XX was reviewed. It included all the detailed process with the signatures of personnel, the final yield was checked.

Blending of batches

Company explained that blending (for example tailings) are not applicable to Rifampicin. In case of tailings those were collected and crystalized.

Reprocessing and reworking

SOP "Procedure for preprocessing and rework of materials" and reprocessed batches registers 2018 and 2019 were checked. Company stated that Rifampicin intermediates and APIs are not reworked.

Recovery of solvents and mother liquor

Company stated that recovery of mother liquor was not applicable for DMF grade Rifampicin. Company also stated that N-N Dimethylformamide was not recovered.

Dedicated solvent recovery plant was available with separate control room as part of the Rifampicin plant.

Validation Master Plan (VMP)

SOP about Validation master plan was available. Facility and equipment qualification, process validation, analytical method validation, analytical equipment qualification, cleaning validation, computerized system validation was in the focus of this document. Description of all systems was done.

Process validation

New process validation was documented in 2015. Updated product quality risk analysis from 2019 was available. Critical process parameters were confirmed.

Cleaning validation

Cleaning validation master plan was provided as annex of the VMP SOP. Dirt hold time and clean hold time studies were done, including microbiologic evaluation.

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Cleaning of the fermenters was done on a batch by batch basis. Sterilization procedure for the content of the fermenter before the start of the process was done. Further evaluation of the cleaning processes / cleaning verification was not done during this inspection.

Hold time studies

Hold time studies were performed as per SOP "Stability studies". Initial Rifampicin-S (intermediate) stability studies (hold time studies) were performed in 2008 up to 24 months. New study was initiated on 30 April 2019 and was in progress during inspection. Batches were placed on the following storage conditions:

- 30 ± 2°C / 65 % ± 5 % RH long term
- 25 ± 2°C / 60 % ± 5 % RH long term
- 40 ± 2°C / 75 % ± 5 % RH accelerated

6M accelerated and long-term studies results were presented to the inspector.

3. Facilities and equipment system

Production premises were located, designed, constructed, adapted and maintained to suit the operations to be carried out. Premises were cleaned according to written procedures, records were maintained. Production buildings were seen to be clean and in good order. Labels attached to the equipment clearly indicated equipment identification numbers, qualification status and due date.

Rifampicin was manufactured in dedicated buildings: fermentation building and synthesis building.

The following products containing the listed API's were manufactured on site:

Name of Product
Rifampicin
Escitalopram Oxalate
Quetiapine Fumarate
Aripiprazole
Clopidogrel Hydrochloride
Lansoprazole
Lactobionic acid
Pramipexole Dihydrochloride monohydrate
Posaconazole
Aprepitant
Tigecycline Hydrochloride
Silodosin
Moxifloxacin Hydrochloride
Rifaximin

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Rifamycin O Pure (Intermediate)
Rosuvastatin.TOA (Intermediate)

Pest control
SOP was presented to the inspector. Pest control system was implemented for all relevant areas to monitor insects, rodents and other vermin. External company was contracted.

Qualification of equipment / utilities
SOP "Qualification of equipment /System" was checked. SOP was applicable for all qualification activities. Impact assessment / risk assessment was part of the URS/DQ phase. Additional regulation about periodic review was implemented. This should be done every three years. If the qualification package for the system does not meet current regulatory requirements, a new qualification must be performed.

Production equipment qualification:
Agitated Nutsche: Complete set of documents was available:
- URS from 2006
- Summary
- PQ was done together with process validation.

Details were not checked during this inspection.

Balances:
Scale with ID XX was used for final weighing of the Rifampicin drums.
Qualification document according to general qualification SOP was available. URS, IQ, OQ und PQ documents were created by the supplier and signed by responsible OLON personnel. Qualification summary report as specified in the SOP and information about maintenance, calibration and verification of the correct function was missed as part of the qualification documents. Calibration of scales was planned with SAP system. This was planned to be done every three months.
Documentation was available. In addition, verification of the balance was documented on a daily basis (before first use).

Utilities
HVAC systems
Brief Description of the Ventilation Systems (AHU Systems) and schematic drawing was part of the SMF. Area for powder processing and filling in the rifampicin synthesis plant was maintained at "Zone E" (ISO class 8). The area under zone E was supplied with air through an Air Handler having 90 % re-circulation and 10 % fresh air. And the area under zone E where solvents were exposed was supplied with air through an air handler having 100 % fresh air. Fermentation microbiology area clean room was provided with air lock (Zone D - ISO 8) and change room. Surrounding of the LAF and airlock 2 was classified as Zone C (ISO 7).

About the HEPA filters: Certificates for H13 filters installed were part of the documentation.

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Pressure differential monitoring was implemented. According to the concept, production corridor was in overpressure with regard to the processing rooms. Airlocks were on lower pressure with regard to the corridor. Airlock in between change room and final airlock leading to production area was under overpressure with regard to the adjoining areas (bubble airlock concept).

Magnehelics were installed in the area showing pressure differences in between different areas.
HVAC system for the classified area in the synthesis building was installed in the service floor.
Drawings, PM label and ID label were attached to the devices.

Prefilters and second filters were installed, including Magnehelic gauges for measurement of pressure differences at the filter.

Water

Incoming water from the central MIDC water supply of this industrial area was treated by filtration and sodium hypochlorite (NaOCl) dosing to ensure potable water specification. This water was used for example in the fermentation area for the preparation of nutrient media. Part of this water was pumped to process water treatment plant situated in the Rifampicin synthesis plant. This water was additional treated with sodium hypo chloride, followed by filtration with 20 Micron filters. This filtered water was supplied for Ultra filtration unit followed by sodium Metabisulfite dosing for removal of free chlorine & 5 Micron filtration. It was supplied to RO System for generation of Process water. This RO treated water was supplied to Storage Tank. Distribution loop was equipped with UV unit for reduction of bioburden. Vent filter for storage tank was installed. Process water was supplied through pump to user points at various locations in plant and circulated back to storage tank.

Schematic diagram for Rifampicin water system was given in annexure of the SMF.
SOP about the water system of Rifampicin synthesis plant and relevant logbooks were checked.
Flowrate and TOC was measured online.

SOP “Sampling and analysis of water” and the relevant documents were checked. SOP describes all the water sampling procedure and the sampling plane; selected points were sampled weekly assuring that the monthly plan covers various sampling points. The production site monitors the physical parameter online continuously for the final sampling point SPXX.

Compressed air

System supplying compressed air for micronization was installed outside from the rifampicin synthesis building.

Nitrogen

There were two systems installed at the dedicated utility building for the Rifampicin plant.
Installation of the Nitrogen generation plant was seen.

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Computerized systems
Validation Master Plan and inventory of GxP computerized systems was prepared according to the relevant SOP. Inventory of GxP computerized systems was given for every relevant section (e.g. QC, Fermentation, IPC, engineering).

SOP "GxP computerized system compliance was available.
Document described the validation approach and how to maintain the validated status of GxP computerized system. GAMP software categories were taken into account.

Laboratory premises
Chemical/instrumental laboratory premises were separated from production areas. Laboratory had adequate space for the orderly placement of equipment and materials and to perform tests. Appropriate specifications were established. Access to lab premises was restricted to authorized personnel.

Rifampicin IPQC laboratory was separated from production area and was in Rifampicin solvent recovery building.

Microbiological laboratory premises were separated from chemical laboratory. Laboratory had adequate space for the orderly placement of equipment and materials and to perform tests. Microbial limit test area was separated from all other microbiological activity (such as media preparation) by cross-over bench.

Laboratory equipment
Analytical balances daily verification and monthly calibration was performed in accordance to USP Chapters 41 and 1251.

The following instrument qualification SOPs were checked:
- "Calibration of HPLC". Calibration was performed annually
- "Calibration of UV spectrophotometer". Calibration was performed quarterly
- "Calibration of FTIR". Calibration was performed quarterly
- "Calibration of Karl Fisher Titrator. Calibration was performed quarterly.
- "Calibration of Aliment GC". Calibration was performed biannually.

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4. Laboratory control system

IPQC laboratory

The following tests were performed in the lab:

- LOD
- Moisture content
- Water content by KF
- Assay and related substances (HPLC)
- Recovered solvents analysis (GC)
- Identification (FRIT)
- Foreign growth management in the fermentation process Test (USP pharmacopeia)

In-process analysis record (IAR) for recovered Methanol was checked along with meta data.

Release procedure

SOP "Release/rejection of intermediate and finished product" and related check lists were checked. BMR and IPC data was reviewed by authorized person from production and IPQC and then sent to QA for review and release.

Analytical protocols were reviewed:

- QC supervisor
- Afterwards reviewed by QA associate

After review document package: BMR + Analytical protocol + IPQC protocol is forwarded to QA manager for final review and release.

Certificate of analysis (CoA)

SOP "Preparation of certificate of analysis" was checked. CoA was prepared by QC supervisor, reviewed by QC manager and approved by QA manager.

Laboratory incidents

SOP "Laboratory incident management system" and register for 2019 were checked. SOP was applicable to QC, IPQC and micro lab and AS&T laboratories. A number of laboratory incidents were checked.

Out of specification/Out of trend/ Out of Expectation

SOP "Handling OOS/OOE/OOT", and SOP "Investigating microbiological, biological, water, air and surface analysis out of specification results", flow charts and registers were checked. SOP was applicable to chemical/physical and microbiological analysis. Several investigation records were checked.

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Stability monitoring

Walk-in and standalone stability chambers were used. T and RH mapping was carried out annually. T and RH was monitored by ICDAS system which recorded T and RH every hour on line. T and RH was also controlled manually twice per day. Chambers were equipped with alarm, system. Alarm system challenge tests were performed monthly.

Rifampicin micronized stability study report SR/M/QA/420/01, batch no B415665 (on going stability) was checked. Rifampicin micronized re-test date was established 12 M. Storage conditions:

- 25 ± 2℃ / 60 % ± 5 % RH
- 30 ± 2℃ / 65 % ± 5 % RH

Sampling of materials and components

SOP "Sampling of raw material, packaging material, starting material, solvents and API" and its flow chart were checked. Primary packaging materials sampling was done in LAF, sample size selected for visual control was according to the AQL inspection level II. Critical, major and minor defects were specified.

SOP "Sampling of intermediate and finished product" and its flow chart were checked. Sampling was performed by personnel from IPQC lab.

Reference materials

Rifampicin working reference (WS) standards were standardized against pharmacopoeia standards annually. WS were dispensed in LAF in amber color vials for use within one month. Usage of reference materials were recorded.

Retention samples

Retention samples were stored in walk-in chamber at T 25 ± 2℃ and RH 60 ± 5 %. Samples were packed in the same packaging system in which the APIs packed for marketing. Samples were stored year after the expiry date assigned by the manufacturer to the batch, or for three years after distribution of the batch, whichever is the longer.

Microbiology laboratory

Reference cultures

Cultures were purchased from the ATTC agents and were aseptically hydrated with a ready media (GPT test was performed for each prepared media) in the laminar air flow benches, passaging activity was limited to maximum of 5 passages. Handling and storing of these culture organisms were controlled according to the SOP\M\QC\261 "Standard practice in microbiology lab".

Microbiology laboratory equipment

Full set of data was available and was checked for calibration for balances, incubators, fridges, laminar air flow benches. Standard weights were externally calibrated according to the External calibration program.

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Autoclaves: there were two separated autoclaves, one for the condemnation of the media and organism and the other one for the sterilization purposes. The annual validation report of the sterilization autoclave was reviewed, and no single data was out of limits.

Environmental monitoring (EM)
Routine environmental monitoring was performed on weekly basis according to the SOP, including plate settling count, air sampler count and glove count. Alert limit and action limits were set based on historical data.

Cleaning of microbiology lab
The microbiology lab was cleaned daily using rotational bacterial and fungal disinfectant such as cetrimide which is not suitable for laboratory using pseudomonas organism.

5. Materials system

Supplier management
SOP b"Supplier (vendor) approval", its flow chart and approved vendor list were checked. SOP was applicable for suppliers of APIs, intermediates, packaging materials, raw materials, starting materials and contract testing laboratories. Audits of KSM/Critical materials/APIs/primary packaging materials were carried according to the schedule:

List of approved vendors for general raw material and packing material was available. Information about the manufacturer was part of the listing.

Warehouse procedures
Warehouse consisted of loading-unloading bay; area to store quarantine materials; released materials, finished goods and packaging materials; sampling and dispensing booths; area for rejected materials. Receiving procedure was explained in SOP "Procedure for receipt and storage of intermediates and finished goods from production". The SOP describes personnel and material movements from the production area to the finished goods warehouse.

After document checks and dedusting materials were transferred to the quarantine area and quarantine (under test) labels were fixed on every container.

Sampling procedure was implemented, and sampling labels were fixed at the relevant containers. Sampling and dispensing booths were installed, and sampling and dispensing area was maintained as per Zone E (IS08) including airlocks for appropriate entry of personnel and materials.

SOP "Storage of material in warehouse" and relevant registers along with area cleaning records were checked.

Receiving of solvents
Solvents were stored at the tank farm. Tanker unloading lines, protected by locks (key with solvent receiving department) were installed and labelled appropriate. SOP "Handling of material received in tanker" was available. Check of the delivery including QC release was part of the procedure.

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Returned products
SOP "Handling of returned goods" and its flow chart were checked. Company stated that in last two years there were no returns.

6. Packaging and labelling system
Packaging and labelling procedure were done in the filling and sealing room in controlled processing area. Semiautomatic filling and sealing station were installed. Rifampicin was packed in polybag and additional aluminium pouch. Packed material was transferred to finished goods stores with quarantine status label.

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, ***Olon Active Pharmaceutical Ingredients India Private Limited,*** located at ***Plot Nos. L-1, L-21 to L-28 & L-44 Additional Phase MIDC, Mahad, Raigad Dist, Maharashtra, India*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines for APIs.

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 GMP Guidelines referenced in the inspection report

1. 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
   http://www.who.int/medicines/publications/44threport/en/

2. 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
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

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