World Health Organization

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WHO Prequalification Unit (PQT) – Inspection Services Team (INS)
WHO PUBLIC INSPECTION REPORT
Finished Product Manufacturer
WHOPIR

Part 1	**General information**
Manufacturers details	
Name of the manufacturer	Cipla Ltd., Verna, Goa (Unit VII PD II)
Corporate address of the manufacturer	Cipla House Peninsula Business Park Ganpatrao Kadam Marg Lower Parel, Mumbai-400 013 India
Inspected site	
Name and address of the inspected manufacturing site if different from that given above	Cipla Ltd., Unit VII PD II, Plot No. S-103 to S-105, S-107 to S-112, L-138, L-147, L-147/1 to L-147/3 and L-147/A, Verna Industrial Estate, Verna, Salcette Goa, PIN: 403 722 India D-U-N-S Number: 650072015 GPS coordinates: Latitude: 15°21'52.8" N Longitude: 73°56'26.3" E
Unit/block/workshop number	Unit VII PD II
Inspection details	
Dates of inspection	From 13 to 17 October 2025
Type of inspection	Routine inspection
Introduction	
Brief description of the manufacturing activities	Unit VII PD II was established in 2016, with a built-up area of 239,164 ft². The facility was dedicated to the manufacture of solid dosage forms, including coated and uncoated tablets.
General information about the company and site	Cipla is a public limited company established in 1935. The company is engaged in the manufacture and distribution of APIs, prescription and OTC products for human and veterinary use, as well as combination products incorporating medical devices. The headquarters are located in Mumbai, where the Corporate Quality Assurance, Integrated Product Development, and Regulatory Affairs functions are based. Research centers for formulation development were located in Mumbai, while API development activities were conducted at facilities in Mumbai, Patalganga, Kurkumbh, Bengaluru, and Bommasandra. Import, export, and distribution activities are monitored from the corporate office.

	Cipla has a global presence with formulation facilities located in New York and Massachusetts, USA; Durban and Johannesburg, South Africa (Cipla Medpro Manufacturing – CMM); Aouda, Morocco (Cipla Maroc); and Qidong City, Jiangsu Province, China (Jiangsu Cipla Pharmaceutical Co., Ltd.). Cipla operates eight manufacturing sites in India. The API manufacturing facilities are located in Patalganga, Kurkumbh, Bengaluru, and Bommasandra, while the formulation manufacturing facilities are situated in Goa, Indore, Patalganga, Kurkumbh, Baddi, and Sikkim. Cipla Goa was situated in a government industrial estate comprising mainly pharmaceutical and electronic industries. The site housed nine formulation manufacturing units, which were in operation for commercial production.
History of Regulatory Inspections	In the past five years, the site has been inspected by various authorities. Unit III, Unit IV, Unit VII, Unit VII PDII & Unit VIII were last inspected by WHO on 18 – 23 March 2019.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Documents reviewed: - Quality management, and related activities - Personnel - Buildings and facilities - Sanitation and hygiene - Documentation and records - Materials management - Process equipment and utilities - Qualification and validation - Change control - Production of exhibition batches and in-process controls - Packaging and labelling of FPPs and intermediates - Storage and distribution - Laboratory controls - Complaints and recall documentation Site areas visited: - General production Unit VII PD II - Warehouses - QC laboratory, including QC-X (For Stability Testing)—Physical, chemical, and Unit VIII (For microbiological Testing) - Water generation system utilities - HVAC system utilities
Restrictions	Not applicable
Out of scope	The inspection focused solely on the product within the scope of inspection. Other products were not covered and were therefore out of scope.
WHO product numbers covered by the inspection	**HA702** Dolutegravir (sodium)/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg

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
BET	Bacterial endotoxin test
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
CPV	Continued process verification
CTG	Corporate technical guideline
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
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	Nonconformity
NCA	National control authority
NCG	Non-condensable gases
NCL	National control laboratory
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
PM	Preventive maintenance

PPE	Personal protective equipment
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
TLD	Tenofovir-Lamivudine-Dolutegravir (product in the scope of inspection)
TOC	Total organic carbon
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer
WFI	Water for injection
YTD	Year-to-Date

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

1. Pharmaceutical quality system

A detailed presentation of the Goa site was provided during the opening meeting.

Cipla's Quality Systems were generally aligned with cGMP requirements and complied with both national and international standards. They were guided by a comprehensive Quality Policy and Quality Manual, defining the organizational structure and core elements of the Quality Management System.

Document management was facilitated through electronic platforms for document issuance and reconciliation. Supplier management was overseen by the Cipla CQA team, with material management executed via the electronic inventory management system. The internal audit function was managed by the Corporate Quality Assurance team.

Training activities were administered electronically through the software System. Quality risk management was conducted using various tools and governed by corporate SOPs in accordance with ICH Q9. There was a centralized electronic platform for managing deviations, CAPA, complaints, QC, and microbiological non-conformances, investigations, and change requests.

The organogram of the Goa site was presented during the opening meeting, and the independence of the Quality Department was verified through its review. The Goa site was

divided into two sections, Site I and Site II. Site II was further divided into several units, including Unit VII PD II, which was the newest part of the site and was used for the manufacture of the product within the scope of inspection. A list of products manufactured in Unit VII PD II since 2019 was available and reviewed; the list included nine products.

Management Review

The Quality Management System was reviewed at three levels. At Level 1, Unit and Site Quality Management Reviews were conducted monthly at each manufacturing unit, attended by key members from Quality, Production, Warehouse, Engineering, IT, and EHS, as well as Unit and Quality Heads from each site. At Level 2, a monthly Quality Council Review was chaired by the Head of Global Quality and attended by direct reports on Global Quality, Manufacturing, and Drug Safety Heads, together with Site and Unit Heads, and other relevant personnel. At Level 3, a quarterly Management Council Review was chaired by the Global CEO and attended by all participants involved in the Quality Council Review meetings.

The SOP governing the Management Review was titled Quality Management Review. The minutes of the meeting held on 12 September 2025 were available, and the corresponding report addressed all topics specified in the applicable SOP.

Handling of deviations

Deviations, suspected product defects, and other issues were reported, investigated, and documented in accordance with SOP for Deviation Handling. The site utilized a system for deviation management.

Randomly selected deviations were verified in the system.

CAPA management

CAPAs were documented in accordance with SOP for Corrective Action and Preventive Action (CAPA).

An appropriate level of root cause analysis was applied during the investigations. The most probable root causes were identified, and corresponding corrective and/or preventive actions were determined and implemented. The effectiveness of the implemented CAPAs was monitored.

CAPAs were randomly selected and verified in the system.

Quality risk management

SOP for Quality Risk Management (QRM) was reviewed. The scope of this SOP was applicable to various aspects of pharmaceutical quality, including development, manufacturing, testing, distribution, inspection, and submission or review processes throughout the life cycle of drug substances, drug products, and combination products. It also covered equipment, facilities, systems, raw materials, solvents, packaging, labelling, and manufacturing operations that could impact the product or process, as well as any activity directly or indirectly affecting product quality or availability across all Cipla sites and associated units. The SOP was aligned with ICH Q9 (R1).

The document for Risk Communication was reviewed to assess the risk of cross-contamination among all products manufactured at the unit.

The evaluation of nitrosamine impurities was conducted in accordance with the applicable SOP. A risk analysis was carried out following the justification for the selection of FMECA, dated 19 July 2023. Prior to the risk evaluation, an assessment of declarations for API, excipients, and primary packaging materials was completed by the site on 19 May 2023, followed by a review of the manufacturing process and interactions between these components by Corporate R&D on 23 May 2025. The risk analysis concluded that four batches were tested, and no nitrosamine contamination was detected. Consequently, the WHO product was considered safe and free from nitrosamine impurities. Two of the batches were tested in January 2024, and the remaining two in June 2024, in accordance with Annexure A17 of the respective SOP. Analytical testing related to the nitrosamine impurities assessment was performed at the QC-X Laboratory, located within the Cipla Goa premises, but in a separate building from QCL Unit VII – PD II.

The observation related to risk management was adequately addressed in the respective CAPA plan.

Product quality review

SOP for Annual Product Quality Review was reviewed. The SOP defined the procedure for preparation, review, and approval of APQRs for drug products, APIs, and intermediates manufactured or packed for commercial or registration purposes at Cipla and associated units. The APQR was intended to verify process consistency, assess specification suitability, identify trends, and support continual product and process improvement.

The Annual Product Quality Review (APQR) for the reporting period from November 2023 to October 2024 was reviewed. The defined tolerance for APQR preparation was two months. The corresponding program was available for verification, and no APQR was found to be overdue.

The observations related to APQR were adequately addressed in the respective CAPA plan.

Process Maps

The manufacturing process map was divided into three sections, namely Part A, Part B, and Part C. Part A described the dispensing and granulation stages, Part B covered the compaction stage, and Part C detailed the blending and coating stages.

Batch release:

SOP for Batch Release was reviewed. A checklist was used to verify the accuracy and completeness of documents and information prior to batch release. The batch release process encompassed the review of manufacturing records, packaging records, and the certificate of analysis. The Head of Unit QA was supported by the Production, IPQA, Analytical QA, and Quality Control teams in performing a preliminary review of the source data. This was followed by the completion of a final checklist to ensure that all aspects, including QMS elements, had been reviewed prior to batch release.

The BMR for a selected was reviewed, and the batch release certificate had been issued manually using a controlled template. The batch analysis certificate was generated through the LIMS system.

Unit Quality Operation Head and Section Head, Quality Assurance were responsible for batch release in accordance with their respective job descriptions.

2. Good manufacturing practices for pharmaceutical products

Cipla Goa had an independent Quality Assurance function responsible for the release of finished products. The site maintained an independent QC laboratory where testing and reporting of quality control results were performed through the LIMS system, and chromatographic data were managed using the respective software System. Stability testing was carried out in a common laboratory located in the QC-X building. An independent microbiology laboratory in Unit VIII performed testing for Unit VII PD II.

The unit operated an independent warehouse for starting materials and finished products, with supplier quality regulated centrally by the Corporate Quality Assurance team at the head office. Material management was controlled through the electronic inventory management system.

The site had an independent water system for the generation of purified water, with the supply sourced from the Industrial Development Corporation treatment plant in Goa and from wells or tankers when required. Unit VII PD II had sufficient air handling units.

The Building Management System was used to monitor and regulate environmental parameters such as temperature, relative humidity, and differential pressure. Utilities, including chilled water and compressed air, were supplied from a common block, and electricity was drawn from the Government Power Grid, with generators and UPS systems serving as backup for critical operations.

3. Sanitation and hygiene

Refer to sections 10 and 11.

4. Qualification and validation

Validation and qualification activities were performed in accordance with established policies and documented procedures. The Validation Master Plan was in place. The VMP outlined the key elements of the qualification and validation program, including cleaning validation. The VMP also included provisions to ensure the maintenance of a continued validation status, encompassing ongoing qualification and validation activities through periodic revalidation and/or annual review as part of continued process verification.

Validation and qualification activities were documented through approved protocols and corresponding reports. The procedure for periodic review was evaluated and verified.

The risk analysis related to the upgrade of the chromatography software system, dated 24 July 2020, was available and reviewed.

A periodic review document for HPLC systems operating with applicable software was available and discussed. The site followed practice of assessing the latest software versions available on the market based on notifications received from the supplier.

The periodic review of the Building Management software system for 2023 was also available and reviewed.

Validation of heating, ventilation, and air-conditioning systems (HVAC)

The HVAC system for solid dosage form processing areas was maintained under ISO Class 8 at rest, applicable also to non-sterile product and microbiology testing areas.

Qualification of HVAC and equipment was managed under applicable SOPs. The periodic performance verification for selected AHUs included standard environmental and airflow assessments, particle counts, and microbiological testing. Airflow visualization was last performed on 8 September 2024 in accordance with the applicable SOP.

HVAC shutdown and restart procedures were defined in established procedures, and cleanroom recovery studies were conducted as per another SOP, establishing recovery times following contamination. Indicator lamps for environmental excursions were qualified with the BMS qualification.

AHU for the Coating Area was selected to be assessed.

Cleaning of 10-micron and 5-micron filters was performed in a dedicated booth in accordance with the respective SOP. Preventive maintenance activities included cleaning of drip trays and sanitization of coils and drains using sodium hypochlorite. During operation, the fresh air damper remained fully open, while the return damper was modulated between 4% and 90%.

The observations related to HVAC were adequately addressed in the respective CAPA plan.

Validation of water systems for pharmaceutical use

Source and Pre-Treatment:

At Cipla Goa 1 and 2, water from the Industrial Development Corporation and well (tanker) supply was stored underground, UV-treated, and chlorinated via an automatic dosing system, maintaining free chlorine at 2.5–3.5 ppm. Potable water was filtered through 10- and 5-micron polypropylene wound filters at user points.

Purified Water System:

The purified water generation system comprised pre-treatment with sequential filtration (20- to 1-micron), SDI filters, softeners, ultrafiltration, and dosing of sodium metabisulphite, sodium hydroxide, and antiscalant. Water was stored in tanks and recirculated through loops at ≥65 °C. The system met TOC, conductivity, and microbiological specifications, and hardness was tested routinely. Automatic flushing occurred every 120 minutes. The RO system was cleaned with citric acid and sodium hydroxide, verified for pH and conductivity, and sanitized weekly at 85 °C.

The alarm log review (from 16 September to the inspection date) showed repeated low UV intensity alerts. Following the 2020 upgrade to hot loop operation at 65 °C (Change Request 1047-S-20-0001), UV lamps became redundant and were removed. A vendor declaration dated 8 July 2024 confirmed their removal had no impact on system functionality or water quality.

Evidence of vent filter replacement and integrity testing in August 2025 was verified.

An impact assessment procedure was implemented for OOS water test results and verified during inspection.

Pure Steam Generator:
Pure steam was generated at 3.0–4.5 bar and 140–155 °C using purified water as feed. Condensate traps were installed throughout the insulated distribution network. Sampling and testing were performed as per SOP for Steam Quality Tests. Condensate was tested weekly for description, BET, TOC, conductivity, pH, and nitrates. Steam quality (superheat, dryness, NCG) was tested every six months. Preventive maintenance included checks on joints, steam traps, flow meters, and pump seals.

The observations related to the water generation system were adequately addressed in the respective CAPA plan.

Validation of Compressed Air for Pharmaceutical Systems
Three central compressed air units were installed, with two units in operation and one maintained on standby. The system operated at a pressure of 7.5 kg/cm² and comprised two central air receivers, along with an additional receiver installed in Unit VII. Three refrigerant dryers were provided.

In Unit VII, post-receiver filtration comprised 20-micron and 5-micron filters without differential pressure indicators, which were cleaned or replaced at defined intervals using compressed air in a designated Filter Cleaning Booth. The user points were equipped with 1-micron and 0.01-micron disposable filters fitted with indicators.

Bioburden testing was performed at generation and user points, including sampling points. Testing covered oil mist, water vapour, particulates, total viable count, and mould count. Oil mist testing was conducted every six months.

The observations related to Compressed were adequately addressed in the respective CAPA plan.

Cleaning validation
SOP for Cleaning Validation and Establishment of Worst-Case Product was reviewed.

Separate SOPs were established for equipment cleaning, line clearance, and operation. A selected SOP was reviewed.

A software was used for cleaning validation and worst-case identification based on solubility, toxicity, and potency. ADE/PDE values were determined by the Corporate Toxicology Unit, and LDD values by the Corporate Clinical team. Strategies for Torsemide, Dolutegravir, and Lamivudine were reviewed, with documentation subject to a three-yearly review.

The justification for using Teepol as a detergent was supported by documentation from 2010 and an updated declaration from December 2024 confirming suitability for pharmaceutical use.

The cleaning sampling plan for the inspected product, including the Rotary Sifter and Roll Compactor, was reviewed. Periodic verification of cleaning validation was performed on one batch instead of three, as required during initial validation.

For WHO product manufacturing, a between-batch cleaning approach was implemented, encompassing 20-batch campaigns as defined in the respective study, applicable to Dolutegravir, Lamivudine, and Tenofovir. Post-campaign cleaning was performed in accordance with established procedures. The campaign cleaning validation report was reviewed, and the latest periodic review dated 22 January 2025 confirmed the effectiveness of the cleaning process. Testing was conducted annually.

All campaign batches were visually inspected for cleanliness and analyzed for related substances and extraneous peaks. The justification for the periodic verification frequency (every third day) was reviewed.

Rinse and swab recovery studies were conducted under the respective protocol. Clean and dirty-hold studies were spot-checked for PMA 1200 L, TLD Product, and Fette 3090i compression machines.

Personnel qualification for visual residue detection was reviewed. The study assessed QA and production staff competence in detecting visible drug residues on various MOC surfaces and defined the Visual Residue Limit (VRL). Training records confirmed evaluation completion on 16 June 2025.

Analytical procedure validation

Analytical procedures were validated in accordance with SOP for Validation and Verification of Analytical Methods to demonstrate their capability to produce consistent and reliable results. A validation report was available for each respective analytical method. Parameters such as specificity, system suitability, linearity and range, precision (system and method), accuracy, robustness, and solubility were verified during the validation of the analytical methods.

Sample solution stability was included as part of the analytical method validation. The documentation reviewed pertained to the Method Validation Report for Dissolution of Dolutegravir, Lamivudine, and Tenofovir Disoproxil Fumarate Tablets (50/300/300 mg) by HPLC. The study demonstrated that the stability of both the standard and sample solutions remained well within the established limits for up to 64 hours.

Validation of computerized systems

SOP for Validation of Computerized Systems was provided and reviewed. The SOP outlined the procedure to be followed for the validation of computerized systems, covering validation, implementation, and maintenance of the system, including infrastructure, network, and server components, up to the retirement stage, to ensure that the system remained in a validated state throughout its life cycle.

In general, the computerized systems used in manufacturing processes were validated in accordance with quality risk management principles, ensuring that the extent of validation was commensurate with the identified risks, system complexity, and intended use. An inventory of the computerized systems utilized onsite was available.

Procedures were established for the computerized systems, defining their use, control, and management. Appropriate segregation of responsibilities between personnel involved in business processes and those responsible for system administration and maintenance was clearly defined. Details of user profiles and access rights for networks, servers, computerized systems, and software were documented. Lists of individual user rights for each software, computer system, and network were maintained within the respective SOPs and were controlled through the change control process.

Appropriate security measures were implemented to prevent unauthorized access, manipulation, or deletion of data within computerized systems. A system for the regular review of audit trails was established in accordance with the applicable SOP, Review of Audit Trail and Electronic Record. Measures were also in place to ensure that audit trails were protected from alteration or unauthorized deletion.

Computerized systems were subjected to periodic reviews to verify that they remained in a validated state and to determine the need for revalidation. The scope and extent of revalidation were defined based on a risk-based approach.

Process validation & CPV

An SOP on ongoing (continued) process verification was reviewed. The purpose of the procedure was to define the process for ongoing (continued) process verification to ensure that manufacturing processes remained in a state of control and maintained their validated status during commercial production.

Ongoing (continued) process verification should be performed for finished products manufactured for commercial purposes. The flowchart of the ongoing (continued) process verification was provided in an annex to the procedure. Critical quality attributes (CQAs), critical material attributes (CMAs), and critical process parameters (CPPs) should be identified by referring to the control strategy document and the respective development documents provided by R&D, including process performance qualification documentation.

Ongoing (continued) process verification was required to be performed throughout the product life cycle. The frequency of monitoring (quarterly, half-yearly, or yearly) was determined based on the Ppk values of the CQAs during APQR preparation.

- **Case 1:** If the Ppk value was ≥ 1.33, this indicated high process performance, and the CPV report was to be prepared on a yearly basis.
- **Case 2:** If the Ppk value was ≥ 1.00 but < 1.33, and statistical evaluation demonstrated adequate performance, the CPV report was to be prepared on a half-yearly basis.
- **Case 3:** If the Ppk value was < 1.00, and statistical evaluation confirmed adequate performance, the CPV report was to be prepared on a quarterly basis.
- **Case 4 (Low performance):** If statistical evaluation did not confirm adequate performance, the CPV report was to be prepared on a quarterly basis, with correlation of the impacted CPPs and/or CMAs with the respective low-performing CQAs.

The process validation for the WHO product was completed on 8 February 2021 using three validation batches. Stratified sampling had not been performed during the validation. However, an approval letter from WHO was received in response to the company's request, authorizing the change to implement a stratified sampling plan for the evaluation of dosage unit uniformity at the compression stage.

Packaging Validation

Three batches completed on 20, 25, and 28 July 2023, respectively, were included in the validation. No deviations were reported.

Acceptance criteria covered container cleanliness, silica challenge, fill count, inspection system challenge, checkweigher performance and reject verification, cap cleanliness, capping torque, induction seal quality, and leak test.

For the secondary packaging area, the evaluated parameters included 2D code and overprinting challenges, absence of labels and overprinting quality, leaflet inserter challenge, and AQL verification. All tests were performed at low, optimum, and high operating speeds.

Transport Validation

A transportation study for shipment to a distribution site in the United States was performed using air transport. The study was conducted on one batch, with dataloggers placed in a defined packing configuration. The temperature limit for the study was set between 15°C and 30°C. The validation covered the route from the manufacturing site to a depot in India and subsequently to a depot in the United States.

A separate temperature mapping study of the container used for shipment from a depot in India to a depot in the United States was conducted on one batch. Dataloggers were included in a defined packing configuration, with temperature limits set at 15°C to 30°C. All results from both studies met the specified acceptance criteria.

The observations related to Process and Transport Validation were adequately addressed in the respective CAPA plan.

5. Complaints

Complaints related to potentially defective products were reviewed in accordance with an SOP on handling product complaints, and corrective actions were taken as appropriate. A designated person, supported by adequate staff, was responsible for complaint handling and decision-making. All complaints were recorded and managed through an electronic quality management system.

The SOP outlined the actions to be taken, including the assessment of potential recalls. Investigations were conducted to determine whether a product was defective, and all complaints were thoroughly documented and reviewed by the Quality Control unit.

Complaints related to potentially defective products were received, most of which were associated with distribution. One complaint was spot-checked. It concerned an adverse event reported by a patient. The patient subsequently switched to another product and expressed appreciation for the response provided. An investigation was performed; a sample was requested from the patient, but was not received.

6. Product recalls

A system was established to ensure the prompt and effective recall of products known or suspected to be defective, in accordance with an SOP governing product recall. The authorized person representing Corporate QA was responsible for executing and coordinating recall activities, supported by sufficient personnel to manage all aspects with the required urgency. The management of recalls was conducted using an electronic system.

No recalls had been initiated at the inspected unit. Recalls had occurred at other manufacturing sites within the company; however, the inspected unit did not have access to those records. None of the recalls were related to the product within the scope of this inspection.

The recall system was periodically tested and evaluated to verify its effectiveness. A testing schedule was established in accordance with internal procedures. Evidence of a mock recall was available and reviewed. Documentation related to the investigation and distribution overview was also provided. Criteria for the selection of mock recalls had been defined and implemented.

7. Contract production, analysis and other activities

A list of contracts was available; however, the site did not use any contract facilities for activities related to the WHO product.

Monitoring of vendors and service providers was performed in accordance with an SOP on supplier qualification and performance monitoring. The procedure established requirements for vendor management of input materials used in finished dosage forms. It applied to the qualification of vendors supplying APIs, critical raw materials, excipients, packaging materials, components of combination products and devices, as well as gases used in feasibility, registration, assessment, and commercial batches of finished dosage forms. The procedure

applied to manufacturing sites within the company and associated sites, as well as to materials purchased for manufacturing at contract manufacturing organizations (CMOs). Materials procured directly by CMOs for products manufactured on behalf of the company were excluded.

For each service provider, a dedicated SOP was established. For the service provider responsible for laundering garments used in the production area, a procedure governing the management of uniforms was applicable. A logbook was maintained to document the number of linen items sent for washing, received, and identified as defective, with laundry collections conducted each morning and evening.

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

This topic was not covered during this inspection.

9. Personnel

At the time of the inspection, personnel were employed across the relevant departments, including Quality Assurance and Quality Control, Production and Packing, Storage and Distribution, and Technical and Engineering.

All personnel were qualified and trained. Supervisory staff held graduate or postgraduate degrees in Pharmacy, Science, or Engineering, while operating staff possessed diplomas in Pharmacy or Engineering.

The site operated under the following shift schedule: General shift from 08:30 to 17:00, First shift from 07:00 to 15:15, Second shift from 15:00 to 23:15, and Third shift from 23:00 to 07:15.

10. Training

Continuous employee training was conducted through an electronic learning management system to enhance competence in performing assigned tasks. Based on the job profile, technical qualifications, and work experience, the type and level of training were determined and organized jointly by the Department Head, Human Resources, and Quality Assurance.

Records of all training sessions and evaluations were maintained. Training on current good manufacturing practices (cGMP) was provided at regular intervals to ensure that employees remained familiar with the applicable requirements.

A random verification of training records was performed to confirm staff training across various functional areas.

11. Personal hygiene

A procedure on personal health and hygiene established hygiene requirements for all personnel in manufacturing areas to prevent contamination. Staff were required to bathe daily, maintain clean nails and hair, refrain from using cosmetics, jewelry, or accessories, and wash or disinfect their hands regularly. Eating, drinking, smoking, or storing food or medication in production or changing areas was prohibited. Direct contact with products without appropriate PPE was not permitted. Clean protective garments and PPE were required to be worn correctly and changed

daily or whenever soiled. Visitors were also required to adhere to the same hygiene practices under supervision.

The observation related to personnel hygiene was adequately addressed in the respective CAPA plan.

12. Premises

The production facility, Unit VII PD II, consisted of multiple operational levels, including the Ground Floor, First Floor, Second Floor, and Third Floor. Each floor was designated for specific manufacturing activities to ensure a logical and controlled process flow.

The production areas were inspected to verify layout, room classification, and design, and to assess suitability and effectiveness in minimizing contamination risks. Equipment was also reviewed for maintenance status and adequacy of cleaning procedures.

Manufacturing of Dolutegravir (as sodium), Lamivudine, and Tenofovir disoproxil fumarate 50 mg / 300 mg / 300 mg Tablets was performed at Cipla Ltd., Goa, Unit VII – PD II. The facility consisted of segregated, classified areas for dispensing, granulation, drying, milling, blending, compression, coating, and packaging. Dedicated HVAC systems maintained the air filtration, pressure differentials, and temperature and humidity control, which were monitored via BMS.

Dispensing and granulation areas contained weighing balances, rapid mixer granulators, and fluid bed processors, supported by lifting and inverting columns. Drying and milling were performed using fluid bed equipment and co-mills with validated filters and sieves. Blending was conducted in octagonal and IPC blenders with controlled operating parameters.

Compression was performed using high-speed tablet presses equipped with dedusters and metal detectors. Film coating was carried out in automated coating systems with controlled air temperature, spray rate, and pan speed.

The packaging area was a separate controlled zone equipped with container filling, capping, labeling, check weighing, and leak testing systems, where in-process controls such as fill weight, torque, metal detection, and label verification were implemented.

The observations related to the premises, particularly those concerning cleanliness, hygienic practices, and maintenance, were adequately addressed in the respective CAPA plan.

13. Equipment

During the inspection, production equipment was visited to assess its suitability, design, and maintenance. The equipment was found to be appropriately located and maintained to support the intended operations. Cleaning and calibration practices were in place, and non-dedicated equipment was cleaned in accordance with validated procedures.

The observations related to equipment were adequately addressed in the respective CAPA plan.

14. Materials

The dispensing area, located on the second floor, was maintained under ISO Class 8, including corridors and cubicles. Three dispensing cubicles were available, each with dedicated material and personnel airlocks.

A procedure governing the dispensing of APIs and excipients was reviewed. Excipients were dispensed first, followed by APIs and colours. API dispensing tools were dedicated and cleaned with 1% Teepol in potable water, rinsed with purified water, and dried using compressed air. Materials handled included starting and packaging materials, gases, solvents, process aids, reagents, culture media, and labelling materials.

The store area comprised receiving, dispatch, and cold storage areas. A procedure governing the receipt of materials was reviewed. Incoming materials were verified for manufacturer details, batch number, expiry date, certificate of analysis, address, and quantity. Vehicle cleanliness and covering were also checked. Materials were cross-verified against the approved vendor list in the electronic system, dedusted, and placed on stainless-steel pallets. Cleaning and waste disposal records were maintained. Materials were quarantined both physically and electronically in the electronic inventory management system.

Sampling was performed through an online conveyor system with entry and exit airlocks and an RLAF-equipped sampling area. Sampling tools were dedicated to APIs and shared for excipients. After sampling, materials were transferred to quarantine status in the Automated Storage and Retrieval System (ASRS) pending testing, and the material status was updated in the electronic inventory management system upon completion.

In-house reference standards, supplied by designated Cipla sites, were used for testing and stored under authorized supervision in controlled conditions. Each standard was labelled with name, batch or lot number, control number, preparation date, shelf-life, potency, and storage conditions to ensure quality maintenance. Reference standards were managed through the LIMS system. Bulk materials were subdivided into vials and stored under authorized control. Records for the receipt, usage, and distribution of a selected Lamivudine reference standard were reviewed and verified in LIMS. The management process complied with an SOP on laboratory reference standards.

15. Documentation

Good documentation practices were implemented under the Quality Assurance system to ensure GMP compliance.

A procedure governing the preparation, review, approval, and control of SOPs and related documents was reviewed. The document management process was handled through an electronic documentation management system.

The management of protocols and reports was defined in an SOP governing the preparation, review, and control of such documents. The procedure covered feasibility, registration, and validation batches; performance and verification studies; validation summaries; and studies

related to deviations, out-of-specification (OOS) results, complaints, and corrective and preventive actions (CAPAs).

Documentation was clear, legible, and systematically organized. Records were completed in real time, and corrections were signed, dated, and traceable. Reviews and updates were performed regularly to prevent the use of superseded versions. Records were retained for at least one year beyond product expiry.

Electronic documentation systems had controlled access, audit trails, and data integrity safeguards. Backup and data retention were managed in accordance with established procedures governing the backup and restoration of electronic data in servers and endpoint systems.

The 2025 backup restoration validation schedule was available. Evidence of the most recent restoration validation, performed in September 2025, included the successful recovery of chromatography data from the backup server.

Testing procedures and specifications were validated, and batch numbers were assigned through the electronic inventory system.

The Data Integrity Risk Assessment (DIRA) was reviewed. The latest assessment, dated 12 June 2024, identified and evaluated potential data integrity risks related to quality parameters, which were found to be satisfactorily controlled.

16. Good practices in quality control

The Quality Control Department, including the Microbiology Laboratory at Unit VIII, was responsible for the testing of raw materials, packaging materials, in-process samples, and finished products. The department was also responsible for conducting environmental monitoring, water system sampling, and stability studies. Applicable SOPs governed all Quality Control activities, including sampling, testing, release, and retention of samples.

Sampling related to cleaning activities and batch sampling was performed by the QA Department. The Microbiology team was responsible for sampling related to environmental monitoring, while the Quality Control Laboratory performed sampling of water. In-process sampling was carried out either by the operator or by QA, depending on the defined sampling frequency. Sampling of finished pharmaceutical products was performed by QA.

Sampling activities were conducted in designated controlled areas under monitored environmental conditions to prevent the risk of cross-contamination. The Quality Control laboratories were equipped for chemical, instrumental, and microbiological testing and were maintained under controlled temperature and humidity conditions. The environmental parameters of the entire facility were monitored through the Building Management System and supported by digital hygrometers, where applicable.

Testing records, certificates of analysis, and other Quality Control documents were maintained in compliance with data integrity principles and were readily retrievable. Laboratory equipment was qualified and calibrated in accordance with an established schedule. Manual integration was not permitted in accordance with the applicable SOP.

Retention samples of each finished product batch and API were stored for at least one year beyond the expiry date in the final packaging and under the recommended storage conditions. All retention samples were maintained in quantities sufficient to permit at least two complete re-examinations, if required.

A procedure governing the investigation of out-of-specification and out-of-trend results was reviewed. A list of OOS cases maintained in the laboratory information management system was available and discussed. One invalid OOS case was randomly selected, and the respective documentation, including the analytical run and associated audit trail, was reviewed. Identified OOS cases were managed through an electronic quality management system. OOS trends, for both valid and invalid cases, were assessed, and appropriate actions were taken as necessary.

A procedure for laboratory incident investigation and resolution was available to document incidents other than OOS/OOT that occurred during the execution of tests in the Quality Control laboratory. Examples were provided to clarify the distinction between OOS/OOT cases and laboratory incidents.

The Quality Control Laboratory cleaning program was reviewed, and it was stated that a dedicated broom should be provided for the handling of broken glassware. The use of instruments was recorded in electronic logbooks implemented within LIMS. Randomly selected instruments were visited, and their verification was discussed.

A stability protocol for the WHO product was available and reviewed. Stability testing for up to 36 months had been performed. The batch used in the study had been manufactured in 2022, and the study was conducted under both accelerated and long-term storage conditions. Samples were stored in the same packaging as intended for marketing. The expiry period was established as 36 months.

The stability chambers were located in QC-X and included ten walk-in chambers, three incubators, and one deep freezer. The storage conditions of each chamber and incubator were defined in terms of temperature range and relative humidity, corresponding to different ICH climatic zones as well as accelerated storage conditions.

A procedure governing walk-in chambers and incubators in the laboratory was reviewed. A number of chambers were available, including units operating at 2–8 °C, 20–25 °C, 30–35 °C, elevated temperatures for stability studies, and a freezer unit. A documented backup plan for the chambers was in place. The alarm system was configured with a defined tolerance period, after which an investigation was initiated if the deviation persisted. Procedures for alarm management were described in the relevant documentation.

Growth promotion testing (GPT) was conducted in the microbiology laboratory in accordance with an established procedure using commercially prepared microorganism pellets. The pellets and rehydration fluid were stored under frozen conditions, with an alternative refrigerated storage range permitted. The defrosting process was automated at defined intervals. A dedicated pass box was available for material transfer. A procedure governing the maintenance and identification of standard cultures specified that each microorganism pellet was single-use and

not refrozen. Therefore, cultures were procured at a defined passage level and no subculturing was performed. Certificates of analysis for the reference strains included relevant details such as passage number, lot number, manufacturing and expiry dates, characterization results, and storage conditions. A backup freezer was defined in the procedure.

A total of 285 environmental isolates were obtained between January and December 2024. The annual trend report was compiled from quarterly data. The isolates were classified as Gram-positive, Gram-negative, moulds, cocci, spore-forming, and non–spore-forming organisms, with further categorization into G+ cocci, G+ spore-forming rods, G+ non–spore-forming rods, G– species, and moulds, including their percentage distribution. Sampling was performed quarterly by isolating all plates from the incubator on a designated day.

The observations related to QCL, including Microbiology laboratory were adequately addressed in the respective CAPA plan.

Miscellaneous	
Samples taken	***N/A***
Assessment of the site master file	The Site Master File (SMF) was submitted and reviewed.
Annexes attached	***N/A***

Part 3	**Conclusion – Inspection outcome**

Based on the areas inspected, the people met, and the documents reviewed, and considering the inspection findings, including the observations listed in the Inspection Report, ***Cipla Ltd., Verna, Goa (Unit VII PD II)***, located at ***Plot No. S-103 to S-105, S-107 to S-112, L-138, L-147, L-147/1 to L-147/3 and L-147/A, Verna Industrial Estate, Verna, Salcette, Goa, PIN: 403 722; India,*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines.

The deficiencies observed during the inspection, as listed in the full report, were addressed by the manufacturer to a satisfactory level before 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 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
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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
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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

9. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-third Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1019), Annex 2.
   Short name: WHO TRS No. 1019, Annex 2
   https://www.who.int/publications/m/item/trs1019-annex2

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
    Short name: WHO TRS No. 1044, Annex 4
    https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/production/trs1044-annex4-technology-transfer-in-pharmaceutical-manufacturing.pdf

11. WHO good manufacturing practices for sterile pharmaceutical products. Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
    Short name: WHO TRS No. 1044, Annex 2
    https://www.who.int/publications/m/item/trs1044-annex2

12. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-first Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. ***Short name: WHO TRS No. 943, Annex 3***
    https://www.who.int/publications/m/item/trs943-annex3

13. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2.
    Short name: WHO TRS No. 961, Annex 2
    https://www.who.int/publications/m/item/trs961-annex2

14. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2.
    Short name: WHO TRS No. 981, Annex 2
    https://www.who.int/publications/m/item/trs981-annex2

15. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3.
    Short name: WHO TRS No. 981, Annex 3
    https://www.who.int/publications/m/item/annex-3-trs-981

16. WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14.
Short name: WHO TRS No. 961, Annex 14
https://www.who.int/publications/m/item/tr961-annex14

17. Good Manufacturing Practices: Guidelines on validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3.
Short name: WHO TRS No. 1019, Annex 3
https://www.who.int/publications/m/item/trs1019-annex3

18. WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4.
Short name: WHO TRS No. 992, Annex 4
https://www.who.int/publications/m/item/trs992-annex4

19. Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9.
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https://www.who.int/publications/m/item/trs961-annex9-modelguidanceforstoragetransport

20. WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5.
Short name: WHO TRS No. 992, Annex 5
https://www.who.int/publications/m/item/trs992-annex5

21. WHO Recommendations for quality requirements when plant – derived artemisinin is used as a starting material in the production of antimalarial active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 6.
Short name: WHO TRS No. 992, Annex 6
https://www.who.int/publications/m/item/trs-992-annex-6

22. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4.
Short name: WHO TRS No. 1033, Annex 4
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23. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
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26. Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 6.
Short name: WHO TRS No. 1025, Annex 6
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27. Production of water for injection by means other than distillation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 3.
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Short name: WHO TRS No. 1025, Annex 4
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29. WHO guidelines for preparing a laboratory information file. *WHO Expert Committee on Specifications for Pharmaceutical Preparations.* Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 13.
Short name: WHO TRS No. 961, Annex 13
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30. WHO good manufacturing practices for excipients used in pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-seventh Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052), Annex 1.
Short name: WHO TRS No. 1052, Annex 1
https://www.who.int/publications/i/item/9789240091030