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

Part 1	**General information**
Manufacturers details	
Name of manufacturer	Strides Pharma Science Limited
Corporate address of manufacturer	Strides House Bilekahalli, Bannerghatta Road, Bangalore – 560076 India
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Strides Pharma Science Limited RS. No: 32, 33, 34, PIMS Road, Periyakalapet, Puducherry 605014, India DUNS: 871402375 FEI: 3012448465 GPS: Latitude North 12.039649 Longitude East 79.855279
Unit / block / workshop number	Formulation Unit (F2 facility)
Inspection details	
Dates of inspection	16 – 20 January 2023
Type of inspection	Routine
Introduction	
Brief description of the manufacturing activities	Manufacture, quality control and release of Solid Oral Dosage Forms: Tablets and capsules
General information about the company and site	The company had a manufacturing experience of 32 years as it was established in the year 1990. The formulation-2 plant was spread over a total land of about 10.86 acres. The production of solid oral dosage forms (Tablets and capsules) commenced in year 2005. The facility was used to manufacture and export pharmaceutical oral solid dosage forms as licensed by the State drug licensing authorities. The manufacturing blocks are independent with separate personnel entry and connected to each other for material movement. The site has been inspected by regulatory authorities and obtained a Good Manufacturing Practices [GMP] approval from the State Food and Drug Administration, Department of Drug Control – Puducherry. It has also been inspected by USFDA, MHRA & OGYEI Hungary. GMP Clearance was received from TGA.

	The site was also previously inspected by the Ministry of Health, Kenya, ANVISA –Brazil, DPM, Republic of Ivory Coast, MCAZ Zimbabwe, FDA-Tanzania, PMPB, Malawi, NDA Uganda & Health Canada. **Major Changes since the last WHO inspection.** 1. Shasun Pharmaceuticals Limited has merged with Strides Arcolab Limited on September 29, 2014, and this merger was effective from November 19, 2015. The Facility name was changed to “Strides Shasun Limited” as part of this merger effective from November 19, 2015. 2. The name of the facility changed from "Strides Shasun Limited" to "Strides Pharma Science Limited" effective from July 18, 2018. 3. Quality Control Laboratory Area Expansion 4. Implementation of new IT applications 5. Electronic logbook (E-Log) was implemented in manufacturing and packaging and is being extended to other areas. 6. Capacity enhancement of Raw Materials and Packaging Materials warehouse 7. Scrap yard area for General waste disposal 8. Paper waste disposal area 9. Bio-metric access implemented for scrap exits 10. Implementation of Building Management System [BMS] 11. Phase-IV area expansion. 12. Implementation of Plant Environmental Continuous Monitoring System (PECMS) 13. Serialization implementation for blister lines & bottle packaging lines. 14. Installation of Bottle Packaging machine 15. Installation of AHU for Coating area 16. Installation of AHU for Packaging area 17. Additional documentation storage area

History

This was the third WHO PQT onsite inspection of this site. The previous onsite inspection was performed on 23 to 25 April 2015.

The following authorities have inspected the site the last 5 years:

Authority	Date/s of inspection	Facility/Block/ Unit covered by inspection	Inspection outcome
USFDA	20 to 24 February 2023	Puducherry (f2 facility)	FDA reclassified the facility from 'OAI' to 'VAI'.
CDSCO, India	17 October 2022	Puducherry (F2 facility)	COPP granted
OGYEI Hungary	26 to 28 April 2021	Puducherry (F2 facility)	GMP Compliant
MHRA, UK	15 to 18 October 2019	Puducherry (F2 facility)	GMP Compliant
USFDA	28 January to 5 February 2019	Puducherry (F2 facility)	Official Action Indicated (OAI)
USFDA	24 to 28 April 2017	Puducherry (F2 facility)	GMP Compliant

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	**Documents reviewed including but not limited** • Job descriptions for key personnel • Personnel training and hygiene • Product Quality Review • Quality Risk Management • Responsibilities of the quality units and production • Complaints and Recalls • Deviation control and change control • CAPA procedure • OOS and investigation • Material release • Self-inspection and vendor qualification • Validation and qualification • Equipment calibration • Data integrity • Sampling and testing of materials • Batch processing records • Materials management system • HVAC system **Areas visited:** • Starting material and FPP warehouses • Tablet and Capsule manufacturing operations • QC laboratories • Stability chambers and retained samples area.
Restrictions	Not applicable
Out of scope	FFPs out of scope of prequalification
WHO products covered by the inspection	TB306 Cycloserine Capsules, hard 250mg HA729 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
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GMP	Good manufacturing practices
GPT	Growth promotion test
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IQ	Installation qualification
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MFT	Media fill Test
MR	Management review
NC	Non conformity
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PW	Purified water

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

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 checked as part of the approval process for batch release. Regular monitoring and reviews of the quality of pharmaceutical products were being conducted according to documented schedules and procedures. A customized software was integrated and used to monitor the different quality management system processes.

Data integrity

The document "Policy on data integrity" was reviewed. This was a high level policy which outlined the key elements to ensure reliability and integrity in the organization. The following among others were explained:

- Data Integrity Risk Management
- Data governance
- Data fidelity
- Electronic Access Security Measures
- Quality Fabric
- Illustration of system design
- Auditing of quality system for data integrity
- Reporting of wrongful acts
- Investigation of wrongful acts
- Disciplinary actions for employees due to wrongful acts
- Data integrity of outsourced services & purchased raw materials
- Employee training
- Numbering of policy on data integrity

The Computer System Validation Master Plan was reviewed.

Data Integrity Risk Assessment (DIRA)
The functional risk assessment for ‘‘Record Management System (RMS)’’ was checked. FMEA tool was used to evaluate risks. The risk analysis scales used for severity, probability, and detectability were described. The functional risk assessment for the following among others was performed:
• Administration – Role management
• Document Issuance and storage
• Retrieval and submission
• Document destruction
• Audit trails

Data backup and recovery management
The SOP “Data backup and recovery management” was reviewed. The SOP explained backup and recovery procedure of all data stored locally and otherwise. Manual backup of manufacturing equipment was performed once in a month.

Disaster recovery and business continuity
The SOP “Disaster recovery and business continuity” was reviewed. SOP explained disaster scenarios and strategy. Disaster management was assessed as part of the data integrity risk assessment. The antivirus had been installed on systems across all strides sites.

Administration & user access control of GxP computer systems
The SOP “Administration & user access control of GxP computer systems” was checked. The username was unique for everyone. The password policy was specified. Access levels for different users were specified. A privilege matrix was available.

Management review (MR)
The SOP “Quality system review (QSR)” was reviewed. The SOP covered review of quality Metrics. QSR was conducted every month. The site QSR was led by site QA Head and Operations Head at a minimum and participated by functional heads at the site as applicable.

The agenda items for Corporate QSR and Quality Forum Review were specified. The management review meeting minutes were reviewed.

Product Quality Review (PQR)
The SOP “Product Quality Review” was reviewed. An annual planner with target dates was prepared by end of December every year and circulated to concerned departments. PQRs were prepared based on a rolling annual plan. A maximum of 30 working days was allowed for preparation and approval of PQR beyond the review period.
Graphical representation of analytical results was used if there were more than three batches. Cpk/Ppk were also calculated.

Quality Risk Management

The SOP "Quality risk management" was reviewed. The SOP was applicable to different stages of the drug product lifecycle. QRM CAPAs were reviewed at the end of every quarter. The General Quality Risk Management Process was defined. The SOP explained data integrity risk management. Annual data integrity risk assessment was performed based on the review of the quality events.

Deviations

The SOP "Deviation management" was reviewed. The SOP was applicable to the following among others:

- Test results of validation samples not meeting the acceptance criteria of protocol, and which are not part of the specification but are observed during testing as per a protocol bound activity
- Non-conformities noted during requalification, calibration, maintenance, cleaning validation etc.
- Any failure to meet the acceptance criteria of a test during performance Qualification and which may have had adverse impact on Quality of product and/ or performance of equipment/ system under qualification.

Deviations were classified:

• Critical
• Major
• Minor

Trends were discussed during monthly Quality System Review meeting. Deviations were trended annually.

Corrective actions and preventive actions (CAPA)

The SOP "CAPA management" was reviewed. When CAPA were identified, a CAPA plan was developed. The development of a CAPA took into consideration information regarding whether the issue had previously occurred, and if so, the way it was previously addressed and whether the actions were effective. Developing an Effectiveness Plan was the QA's responsibility. The CAPA log for 2022 was presented and selected CAPA records were reviewed.

Change control (CC)

The SOP "Change management" was reviewed. The different types of changes were defined. Change controls were initiated & handled through an electronic system. QA personnel were responsible for review of the changes. Risk assessment was mandatory in case of major or moderate changes. For minor changes, it is not mandatory to perform a risk assessment, but it could be done based on the nature & scale of change. Selected change control records were reviewed. Change controls were trended annually.

Complaints

The SOP "Management of market complaints" was reviewed. When a complaint was received either through verbal, electronic or written mode or complaint reporting form, or any notification from regulatory agencies, complaint coordinator was responsible for logging the complaint in the complaint login system. Timelines for handling complaints were defined. Received complaint was forwarded to QA within one working day of receipt of the complaint. Complaints were classified as:

- Critical
- Major
- Minor

The complaints register for 2022 was checked. Complaints were trended annually. Selected records were reviewed.

Recalls

The SOP "Product recall" was reviewed. Responsibilities were defined. Recalls were categorized. Recall effectiveness was checked by Mock recall once in a year. A mock recall was initiated in the last 6 months of a year if no recall was initiated in the preceding period of the year.

Documentation

The SOP "Document management" was reviewed. All controlled documents copies were issued by QA. Documents retention periods were specified.
SOP "Management of standard operating procedure" was checked. SOP explained SOPs preparation in the electronic software.

Internal Audit

SOP "Internal audit and compliance monitoring" was reviewed. Annual audit plan for the following year was prepared in the month of December. "Internal Audit Booklet" (Check list) was used to conduct an audit. Observations were classified as:

- Critical
- Major
- Minor
- Recommendations

According to the SOP:

The audit of each system also includes verification of data integrity. Locations handling multiple regulated markets were audited three times per year. The Puducherry formulation site was audited as scheduled in March, July and November 2022 and the corresponding reports were available. Selection of auditors and qualification were explained. The "Internal Audit Booklet" (Check list) was used to conduct an audit. The Booklet was dedicated to each department and elements.

Vendor qualification

The SOP "Selection and evaluation of vendor" was reviewed. This SOP explained selection and evaluation of raw materials, packaging materials and consumables manufacturers/distributors.

The SOP "Vendor audit" was also reviewed. The criteria for selecting auditors, auditors' qualification and re-qualification program was specified. Annual audit plan was prepared before the beginning of the calendar year, based on:

- Qualification of new vendors or qualification of existing vendors with new items
- Requalification based on the pre-defined criteria

Periodic re-audit was performed once every three years for Non-Sterile Components (RM/PM) materials vendors. Audit was performed using Vendor Audit Booklet (check list). The vendor audit plans for 2022 and the first quarter of 2023 were available. Vendors of API were audited every 3 years.

Review of analytical records

The SOP "Review of analytical records" was reviewed. Analytical data was checked, reviewed, and approved by a different person other than the person performing the test, a check list was used. Analytical Quality Assurance personnel checked and confirmed the data recording, calculations and result recording for correctness, completeness, and accuracy.

Batch release

The SOP "Creation and release of process order" was checked. The Procedure explained creation & release of process order in SAP system.

The SOP "Batch release" was reviewed. Head QA or designee was responsible for the release/dispatch of finished product. The SOP explained the release procedure for:

- Intermediates
- Bulk Finished Product for Packaging
- Packed goods
- Finished Product for Dispatch
- Batch Release and Dispatch of the product

The Batch release procedure was demonstrated in SAP.

The SOP "Testing approval and disposition on in-process, semi-finished and finished goods" was also reviewed. Timelines for completions of received samples for analysis and microbiology testing were defined.

Returned drug Products

The SOP "Handling of returned drug products" was reviewed. The Procedure explained receipt, handling, storage, packaging, resale, or destruction of returned drug products. The Returned products were transferred as per their storage requirements to respective areas provided for returned drug products in finished goods warehouse and investigated thoroughly by the respective QA Head along with concerned departments. The relevant records of returned products were reviewed.

BMR/BPR

The SOP "Control of documents" was reviewed. The complete BMR and BPR were reviewed by the production head/designee by using a check list, afterwards QA review was carried out using the same check list. After completion of QA review, the batch was released in SAP. Selected batch records of Dolutegravir (sodium)/Lamivudine/ Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg tablets were checked.

Contract laboratories

The SOP "Selection and evaluation of external service provider" was reviewed. The SOP explained the selection and evaluation of:

- Pest and rodent control activity
- IT Vendors – (GxP systems / new projects / new applications)
- Calibration
- Clinical and analytical testing
- Transporters
- Warehouse
- Document storage etc.

Selected audit reports were reviewed.

Training

The SOP "Training" was reviewed. It explained training of all permanent & contract employees directly or indirectly involved in the development, manufacturing, processing, and packaging or holding of materials / products and all supporting functions.

The following training modules were provided:

- Online Training (e-learning/Self-study)
- Instructor Led Classroom Training (ILC)
- On The Job training
- Event Based/Need based training
- External Training

Training assessment was done by multiple choice questions and open questions. Acceptance criteria for written assessment of training was 100%. For practical evaluations, the acceptance criteria were "Satisfactory". Training effectiveness monthly report was presented in the Site Quality System Review.

The SOP "Technique evaluation of analyst" was also reviewed. Analyst Qualification was carried out after completion of SOP training and On-job training.

The Analyst Evaluation and Certification by analysing a recently approved sample were based on:

- Results reported by the analyst meeting the acceptance criteria for each Analytical technique
- Good Laboratory Practice
- Good Documentation Practice

Qualified analysts had to undergo a re-evaluation for a minimum of three tests once in 3 years based on the job role. The reviewer qualification was also explained.

Personnel Hygiene

The SOP "Personnel hygiene and medical examination" was reviewed. The SOP was applicable to Permanent and Contract Employees. The HR Head was responsible for review and implementation of the personnel hygiene and periodic medical examination. Standard hygiene requirements were explained.

All personnel who were related to GMP should undergo a medical examination upon recruitment and periodic medical examination once per year. Training records of selected staff were reviewed.

2. Production system

Process validation

The SOP "Process validation" was reviewed. The SOP was applicable to process validation of both new and legacy products.

Process validation of any new product consisted of three stages:

- Stage-1: Process design
- Stage-2: Process Qualification
- Stage-3: Continued Process Verification

The SOP explained hold time studies and established the time limits for holding the materials at different stages of production:

- Binding Solutions
- Coating Solutions
- Gelatin Mass
- Semi-Finished Products

Continuous process verification

- Preparatory phase

It include a risk assessment of process parameters of all unit processes and quality attributes and the determination of critical process parameters (CPPs) and Critical Quality Attributes (CQAs).

- Process performance exercise:

Products with 25 or less batches manufactured (considering all strengths together) per year were trended for CQAs on real time basis. For products with annual manufacturing of more than 25 batches (considering all strengths together), process performance (one time exercise) was performed using minimum of 25 consecutive batches (retrospective or prospective batch data)

The hold time study report and raw data for selected products were checked.

The critical material attributes were monitored.

Transfer of Technology

There was transfer of technology (TOT) for the manufacture of Dolutegravir (sodium)/Lamivudine/ Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg from the Strides site at Bangalore to the Strides site at Puducherry.

The SOP "Product Transfer to manufacturing site" was reviewed. Three of TOT stages were described:
"Gap analysis for the manufacture for Dolutegravir (sodium)/Lamivudine/
Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg" was checked.

The process performance qualification protocol was reviewed. The sampling plan, process parameters, acceptance criteria were clearly defined and the checklist for execution of validation batch and report were reviewed and found satisfactory.

The Analytical Method Transfer Report for Dolutegravir (sodium)/Lamivudine/
Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg was also checked. The methodology used at both labs (i.e., Strides, Bangalore and Strides, Puducherry) was the same. The results of the analytical data were well within predefined acceptance criteria.

Cleaning validation
The SOP "Cleaning validation" was reviewed. The SOP was applicable to all product contact manufacturing equipment/ equipment parts.
Cleaning procedures were divided into two types based on the extent of cleaning:
• Cleaning during campaign (also called as serial cleaning)
• Cleaning during product change over (also called as non-serial cleaning).

According to the SOP:
Health-Based Exposure Limits (HBEL) were determined by a person who had adequate expertise and experience in toxicology/pharmacology, familiarity with pharmaceuticals as well as experience in the determination of health-based exposure limits such as Occupational Exposure Levels (OEL) or Permitted Daily Exposure (PDE). Where experts are contracted to provide the HBEL, contractual agreements were in place prior to work being conducted.
MACO was calculated using validated excel sheet. For all equipment a worst molecule (marker compound) was identified based on the solubility. Wherever detergents were used in the cleaning process, their removal should be demonstrated. Cleaning validation of detergents was based on toxicity of the detergents being used and Allowable Daily Intake (ADI) derived specifically for detergents.
Analytical methods were developed and validated prior to execution of cleaning validation. Sampling methods were defined:

The Cleaning validation matrix was checked. The identified worst-case molecule had been determined. The Cleaning validation protocol for the coating solution preparation vessel and the cleaning validation report for the coating solution preparation vessel were checked. The criteria for selection of the hard to clean areas, cleaning agents and sampling approach were defined. The results met the defined specifications.

3. Facilities and equipment system
The inspectors visited the Pilot plant where Cycloserine Capsules, hard 250mg commercial batches and Dolutegravir (sodium)/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg submission batched were manufactured.

Production rooms were seen to be clean and in good order. Only stainless steel 316 equipment was used. On shop floors, only electronic logbooks were used. BMR/BPRs were paper based documents.
The Inspectors visited:

- Batch staging rooms. Dispensed products were placed in locked metal cages – one product one batch in the cage.
- Dispensing rooms
- Wet granulation

Shifting

- Mixing
- Drying
- Milling
- Blending
- Equipment washing
- Compression
- IPQC: The following tests were performed: uniformity of weight, hardness, thickness by using multi-check equipment, friability, and leak test. Multi-check equipment was also used in compression cubicles
- Coating
- Encapsulation
- Tablet/capsule inspections
- Spare part rooms
- Primary packaging:
- Blister
- Bottles / Bulk packaging
- Secondary packaging

Equipment qualification/maintenance

The maintenance of production equipment and IPQC laboratory equipment was monitored using SAP. The maintenance records for the compression machine and Capsule filling machine were checked. The maintenance of the equipment was performed as scheduled.
The SOP for Calibration was checked. The calibration master plan for the year 2023 was in place.
The calibration reports for the following equipment were checked.

- Standard weights
- HPLC
- Multicheck
- Friability Tester
- Tachometer

Utilities

HVAC

97 AHUs were installed to supply air to production, packaging, and warehouse areas. Filter cascade for processing areas was EU4→EU7→terminal HEPA filters. For some areas as change rooms/washing area HEPA filters were installed in plenum. Primary and secondary filters were cleaned in separate area (not visited). HVAC system was provided with sound and light alarm system. HVAC system was seen to be clean and in good order.
The SOP "Performance qualification/re-qualification of HVAC system" was reviewed.

Re-qualification reports of selected AHUs were checked.
The SOP "Environmental monitoring (EM)" was checked. SOP explained routine monitoring of environment using microbiological methods in the controlled environments. The following methods were used on site:
• Active Air Sampling
• Surface monitoring
• Contact plate method

Action and alert limits were specified based on historical data. Active air sampling for all sampling points was done monthly.

The SOP "Microbial trend analysis" was checked. SOP was applicable to the trend analysis of Microbiological monitoring of air, water, and compressed gases. Trends were prepared for all the sampling locations.

Purified water system
The inspectors visited the water purification plants: the Reverse Osmosis (RO) plant (pre-treatment) and the Ultrafiltration plant. pH and conductivity were measured online. Afterwards water was circulated to the ultrafiltration water treatment plant. Treatment: RO→ Electrodeionization →Demineralized water →Ultra filtration→PW. There were two PW loops. Conductivity, TOC, flow rate and UV working hours and UV intensity were measured online. Both water systems were seen to be clean and in good order.

The SOP "Monitoring of water system" was checked. The SOP was applicable to Purified water system, De-mineralized water system, Hot Demineralized water system and Raw water system that includes generation, storage, and distribution system. Action and alert limits were specified for different systems. The PW was sampled daily from different defined locations.

The Schedule for December 2022 was presented and checked. Quarterly trends for PW return loops and sampling points were checked. No excursions were reported.

Temperature Mapping
The SOP "Temperature and relative humidity mapping of room/area" was reviewed. The SOP was applicable to various rooms/areas which were intended to be used for storage of Products, Raw materials, semi-finished goods (e.g., RM storage area, PM stores, Product quarantine area, Day store, Finished product store.). Temperature (T) & Relative Humidity (RH) mapping was conducted with loaded condition for two worst case scenarios based on the seasons e.g., monsoon RH, winter & summer T.

Documentation archive
The inspectors visited the documentation archive. Documents were stored in mobile racks in a fireproof room.

Laboratory premises

The inspectors had a quick tour in QCL. A schematic drawing laboratory was in place. Automatic glassware washing equipment was used. Volumetric glassware was dried at 60 °C. Class "A" volumetric glassware was used. Volumetric flasks and pipettes had unique identification numbers. Columns were stored in metal cupboard. Equipment had unique ID numbers and labels indicating calibration status, date of calibration and calibration due date.

The Microbiological laboratory (MB) was not visited. According to the schematic drawing MB had biosafety cabinet and RLAF cabinet. Work with master strains was performed in biosafety cabinet.

4. Laboratory control system

The SOP "Handling of raw data sheet, assigning test, results recording and disposition" was checked. The SOP explained the procedure for handling the raw data sheet, assignment of tests to qualified analysts, result entry, review, and disposition of samples. ERDS – electronic records data sheets were used to record analytical results.

Analytical reports for Dolutegravir (sodium)/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg tablets were checked. No paperwork was used in the laboratory. The SOP "Management of Chromeleon chromatography data station (network)" was checked.

The SOP "Handling out-of-specification results" was also reviewed.

The SOP explained:
• Identification of OOS
• Phase I Investigation
• Phase II Investigation

The OOS results were categorized monthly and were presented as part of Site Quality System Review. The OOS annual trend report was prepared by QA. The OOS register from 2018 up to date was presented. Selected OOS investigations were reviewed.

OOT management

The SOP "Handling of out of trend results" was reviewed. OOT investigation was very similar to OOS investigation:
• Identification of OOT
• Phase I investigation
• Phase II investigation

OOT trends 01 Jan -31 Dec 2021 were presented and discussed.

Laboratory Analytical Standards

The SOP "Handling and maintenance of laboratory analytical standards" was checked. Standards were stored in locked chambers. The temperature of the chambers was monitored.

The SOP "Bracketing of standards and general system suitability criteria during analysis" was reviewed. This SOP explained bracketing of standards and general system suitability criteria during analysis and Good Chromatographic Practices.

Stability testing

The SOP "Receipt, incubation and withdrawal of stability samples" was checked. Stability samples were collected by QA/ Formulation Department (FD) stability personnel according to stability planner.

The SOP "Designing and handling of stability protocol" was checked. The procedure was applicable, but not limited to:

- Exhibit batch / Validation batch
- Products that were presently being marketed commercially (Ongoing / Annual stability)

Conditions applicable for different stability studies were defined.

Retention samples

The inspectors visited the retention samples room. Retention samples were stored in mobile racks at T 15 – 25 °C. T was recorded every 60 seconds, records were checked daily. RH was recorded only for information.

T mapping protocol/report for Retention (reserve) sample room was checked. Hot spots were identified.

Laboratory equipment

The laboratory equipment complied with data integrity requirements.

The Liquid Chromatography with high-resolution mass spectrophotometer qualification report was checked.

Analytical raw data sheets for selected batches of Tenofovir DF/Lamivudine/ Dolutegravir tablets 300mg/300 mg/50 mg, were reviewed.

5. Materials system

The inspectors visited Raw materials, packaging materials and finished goods warehouses. Warehouses were observed to be kept clean and in good order. The SAP system was used for materials management. No labels, except bar code labels were used. Upon receipt goods were de-dusted and weighing was performed. Three (3) sampling RLAF booths were provided for raw materials sampling. Goods were stored in T&RH controlled warehouses and in cold room (chamber) 2 – 8 °C. T and RH was monitored and reviewed once per day.

Primary packaging materials were sampled/dispensed under RLAF. Printer packaging materials were stored in locked warehouse. After dispensing printed packaging materials were placed in locked cages and transported to the production department.

Rejected materials rooms were provided for raw materials warehouse and packaging materials warehouse. For returned products, locked room was provided in packaging material's warehouse

The SOP "Sampling, testing and approval of packaging materials" was reviewed. SOP was applicable for:
• Primary packaging materials
• Secondary packaging materials
• Tertiary packaging materials

Sampling was performed following AQL.

The SOP "Sampling, testing and approval of raw materials" was reviewed. The SOP explained in details sampling procedure for:
• Microbiology Sample
• Retest Material
• Code transfer/Stock transfer Material
• Miniature Sample (sample received along with consignment which is sampled by manufacturer as batch representative sample
• Hermetically Sealed Containers

The SOP "Sampling and in-process checks by QA" was reviewed. SOP explained In-process checks by quality assurance of manufacturing and packaging activity. In-process samples were collected by QA personnel. SOP explained routine sample collection process and detailed sample collection/labelling process for validation batches.

6. Packaging and labelling system
The manufacturer had both bottle and blister packaging lines The bottles were cleaned with compressed air. The secondary blister packaging line was equipped with a camera, bar code reader. The information leaflets were inserted manually. Secondary packaging of the blisters was also performed manually. QA carried out in process checks at different stages and defined frequencies. These in-process checks were recorded in the batch packing record.

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, ***Strides Pharma Science Limited, located at RS. No: 32, 33, 34, PIMS Road, Periyakalapet, Puducherry 605014, India*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines.

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

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

Part 4	List of WHO Guidelines referenced in the inspection report

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO TRS No. 986, Annex 2***
   https://digicollections.net/medicinedocs/documents/s21467en/s21467en.pdf

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***
   untitled (digicollections.net)

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