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Prequalification Unit Inspection Services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Active Pharmaceutical Ingredient Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	Styrax Pharma Pvt Ltd
Corporate address of manufacturer	Plot No. 97 & 98 SS Arcade, 4th Floor, Guttalabegumpet, Madhapur, Hyderabad Telangana 500 081 India Telephone: +91-40-4858 3333 Fax: +91-40-4858 3339
Inspected site	
Name & Address of inspected manufacturing site	Plot No. 27B, Jawaharlal Nehru Pharma City, Parawada, Anakapalli Andhra Pradesh 531021 India Longitude: 80°04'47.44"E Latitude: 17°39'30.7"N FEI Number: 3014406503 DUNS Number: 87-180-2852
Synthetic Unit /Block/Workshop	➢ Production block I ➢ Production block II
Inspection details	
Dates of inspection	6 – 8 June 2024
Type of inspection	Routine GMP inspection
Introduction	
Brief description of the manufacturing activities	The Styrax Pharma manufacturing site is engaged in the development and production of Active Pharmaceutical Ingredients (API) and API intermediates. No products belonging to the categories of cephalosporin, sterile, cytotoxic, pesticides, or agrochemicals are being developed or produced. The site is also engaged in contract manufacturing services for different APIs and API intermediates.
General information about the company and site	Styrax Pharma is a pharmaceutical manufacturing company with a multi-product manufacturing facility and the capabilities to manufacture a diverse range of APIs / intermediates. Styrax Pharma was incepted in 2014 and commenced its operations in November 2015. The manufacturing site is well connected to the Airport and Seaport. The site is certified for ISO 9001, ISO 14001, and ISO 45000. The Pharma City provides infrastructural facilities like water supply, common effluent treatment plant, hazardous waste management, and marine outfall to discharge treated effluents.
History	The site has been subject to regular inspections by the Indian drug regulatory authorities, as represented by CDSCO and local state authorities. In 2018, the US Food and Drug Administration also inspected the site regarding the manufacture of CHE-II (Lamivudine Intermediate).

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Pharmaceutical Quality System Documentation Facilities and Equipment (warehouses, workshops) Utilities Production Packaging and labelling Product Release Quality Control laboratories
Restrictions	N/A
Out of scope	APIs not submitted to WHO Prequalification were excluded from the scope of this inspection. In addition, lines and areas not listed under the scope of this inspection were not covered during the inspection and are out of the scope of this report.
WHO APIs (including WHO API or APIMF numbers) covered by the inspection	➢ WHOAPI 480, APIMF 480 Emtricitabine, finished API (for HIV) (denoted by the company as ETN) manufactured at production block II. ➢ WHOAPI 429, APIMF 429 Tenofovir disoproxil fumarate, finished API (for HIV) (denoted by the company as TDF) manufactured at production block II. ➢ WHOAPI 489, APIMF489 Lamivudine, critical intermediate (for HIV) (denoted by the company as CHE-II) manufactured at production block I. ➢ WHOAPI 450, APIMF 450 Dolutegravir sodium, finished API (for HIV) (denoted by the company as DRS-IV) manufactured at production block II. ➢ WHOAPI 442, APIMF 442 Bedaquiline fumarate, critical intermediate (for Tuberculosis) (denoted by the company as BQL-I) manufactured at production block II. ➢ APIMF 039, Emtricitabine, critical intermediate (for HIV) (denoted by the company as FCC-I) manufactured at production block I. ➢ APIMF 165, Emtricitabine, critical intermediate (for HIV) (denoted by the company as FCC-I) manufactured at production block I. ➢ APIMF 346a, 346b, Lamivudine critical intermediate (for HIV) (denoted by the company as CHE-II) manufactured at production block I. ➢ APIMF 362, Dolutegravir Sodium, critical intermediate (for HIV) (denoted by the company as DTI-I) manufactured at production block II.
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
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
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
KF	Karl Fisher
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
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
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 management

Principles, quality manual (QM) and quality policy (QP)

The integrated management system manual was reviewed, and the site had obtained the following certificates: ISO 9001:2015, ISO 14001:2015, and ISO 45001:2018. The manual focused on ISO 9001 requirements and minimally addressed the pharmaceutical quality system.

Quality unit (QU)

The site's organizational structure was presented and was generally acceptable. Production and quality control operations were independently managed and specified in written form. GMP requirements were essentially being met. The quality unit was responsible for maintaining and improving the quality systems, procedures, standards, implementation of cGMP, and the quality of the products. Head Production and Head Quality positions were separate, with independent responsibilities.

Management review (MR)

The management review followed the procedure which required MR to be performed every six months. Senior Management demonstrated a commitment to the QMS by granting adequate resources to implement, support, and manage it. The records and participant list of the last MR meeting were checked. The meeting discussed customer feedback, complaints, product conformity, deviations, OOS, and trend data.

Quality Objectives

Integrated management system objectives and action plans were in place.

Product quality review (PQR)

The PQR procedure was in place, and the purpose and application of the procedure were described. Various elements of quality systems and products were reviewed annually (from January until December) and completed within three months according to the procedure. Process capability was manually calculated. Cpk greater than 1.33 was considered robust, and Cpk between 1 and 1.33 was considered marginally capable. The Quality Assurance Department was responsible for conducting PQRs. The PQR reports were reviewed by the responsible QA personnel, and statistical analysis was performed on critical process parameters and product quality attributes if 30 or more batches were manufactured during the review period.

The PQR of the following products were checked:

- PQR of Dolutegravir sodium, finished API (for HIV) covering the period from January to December 2023.
- PQR of Dolutegravir Sodium (DTI-1) critical intermediate (for HIV) covering January to December 2023.
- PQR of TDF-I covering the period from January to December 2023.
- PQR of TDF-I covering the period from January to December 2022.

Quality risk management (QRM)
Quality risk assessment was handled and performed according to a well-established procedure. The risk priority number was determined based on probability (P), occurrence (O), and severity (S). The risk assessment register for 2024 was checked. In general, appropriate instructions were included in the relevant SOPs for the identification, assessment, control, communication, review, and mitigation of risks. The report for Nitrosamine Impurities in Tenofovir Disoproxil Fumarate Drug Substance was reviewed.

Deviations
Procedure for reporting, investigating, and resolving non-compliances, failures, events, and deviations in a timely manner, was in place. The QA coordinator was responsible for evaluating the completeness and correctness of the incident reports. Investigations had to be completed within the given timelines, and appropriate CAPA had to be applied. Events were trended every six months. Deviations were classified as critical, major, or minor. According to the SOP, investigations were to be closed within 30 days for all deviations. Trends for deviations from July 2023 to December 2023, were reviewed.

Internal audit (self-inspection)
The self-inspection procedure described the objective, scope, reference document, definitions, procedure, etc. The self-inspection was performed twice a year, and a schedule for 2023 was presented. The observations were classified as major or minor. A checklist was used to conduct self-inspections.

CAPA management
CAPA procedure was reviewed. The procedure described the steps for identifying and implementing corrective and preventive actions in relation to non-conformances, complaints, deviations, OOS, audit findings, change control, OOT, laboratory incidents, and annual product reviews. Logbook of CAPAs registered between 2022 and 2024 was reviewed and example CAPAs were spot-checked.

2. Personnel

Personnel qualification
Styrax employs approximately 249 fulltime employees in addition to 50 staff who were contracted. The responsibilities of the personnel and their specific duties were recorded in written job descriptions. Personnel interviewed during the inspection were aware of the principles of GMP. The job descriptions and responsibilities for key personnel in Quality were reviewed.

Personal hygiene
A well-established procedure on personal hygiene was followed. Personnel were required to wear protective clothing suitable for the type and stage of manufacturing. Suitable sanitation and change room facilities were provided. Smoking and eating were not permitted in manufacturing areas.

Consultants
The training was managed according to the respective procedure. Training was divided into several types, including induction, initial, functional, specific, external, and safety training. The training was evaluated through questionnaires and written tests according to the respective format, and a passing grade of 80% was set. Assessment records following training were available. The analyst qualification matrix for the year 2024 was checked. The matrix was updated every two years: Training records were checked.

3. Buildings and facilities

Design and construction

The buildings and facilities inspected were designed and constructed to facilitate cleaning, maintenance, and operations as appropriate to the type and stage of manufacture. Manufacturing areas provided good space for the installation of equipment.

The site comprised three production blocks apart from the warehouses, QC, QA and administrative facilities along with utilities (water generation system, HVAC, compressed air, and nitrogen gas generation). The manufacturing facilities were multi-product and not dedicated. The synthetic processing steps and purification were performed in the chemical area, followed by drying and packaging, which were performed in a Grade D areas at production block II.

Utilities (e.g. steam, gases, compressed air, and heating, ventilation and air conditioning [HVAC] system)

HVAC

The SOP for environmental monitoring (EM) in clean rooms was in place. The procedure provided for regular monitoring of the environmental conditions of the cleanrooms at production block II. The annual schedule for EM in 2024, considering the frequency of once every three months for passive air sampling (settle plates) and once every 6 months for active air sampling, was reviewed. EM results for the year 2023 were spot-checked.

Nitrogen system

The layout of the nitrogen generation system was reviewed, and the respective utilities were visited. Equipment was noticed as clean and properly maintained, and the necessary calibrations were in place. The nitrogen generation system was relocated from the ground floor to the first floor of the utility block II. This change was controlled through change control, including requalification of the system. The installation requalification report and the operational requalification were reviewed. Nitrogen was tested on an annual basis as per Eur. Ph. monograph reference no. 1247 and ISO 8573-1 and Indian Standard IS 1747. Tests included oxygen concentration, nitrogen concentration, carbon monoxide concentration, carbon dioxide concentration, hydrocarbons, particulate matter, oil mist, dew point and viable count.

Water

SOP for the operation of purified water (PW) was reviewed. The PW system is equipped with an online conductivity meter where water was dumped if the online monitoring detected values higher than 1.2 µS/cm. SOP for water sampling and analysis was in place. The purified water monthly trend for May 2024, as well as the yearly quality report for 2023, were spot-checked. Alert and action limits for total organic carbon (TOC), conductivity, pH and total microbial count were established based on a system qualification and comprehensive studies where limits were justified.

Sanitation and maintenance

In general, the premises was properly sanitized and maintained. The SOP for housekeeping and sanitization in the warehouse as well as the SOP for general cleaning of manufacturing areas were reviewed.

4. Process equipment

Design and construction

The equipment used in the manufacture of the API and intermediates appeared to be of appropriate design and size for its intended use. In general, cleaning and maintenance appeared satisfactory. In many instances, manufacture and material transfer took place in closed systems.

Equipment installed in the production plants visited was multi-purpose, and each piece of equipment had a unique identification number. The measuring equipment were labeled, including calibration status. The inspected equipment appeared to have a suitable design and construction for the allocated process in general.

Equipment maintenance and cleaning

The equipment maintenance and cleaning were appropriately established. The SOP on preventive maintenance was in place. The annual preventive maintenance schedule in 2024 was spot-checked and examples preventive maintenance of few equipment were checked.

The re-qualification and initial PQ reports of a fluid bed dryer were reviewed. The FBD was used for the manufacture of Tenofovir API only. Four HEPA filters were installed in the FBD (2 for supply and 2 for exhaust). Filter change was scheduled every 5 years. Filter integrity (PAO test) was scheduled every year, and evidence of this was presented. Preventive maintenance was scheduled every 6 months.

Calibration

In general, the calibration program was properly established and maintained at the site. The SOP for calibration of mechanical measuring instruments was in place. Calibration certificates of the pressure and temperature sensors of the FBD in 2023 and 2024 were spot-checked and found satisfactory.

Computerized systems

Few computerized systems were used at the site, including LabSolution for chromatographic systems and ASDASS for stability chambers. These were generally well-maintained and qualified. The SOP for computerized system validation was in place. The SOP for data backup and restoration was reviewed. The risk assessment of LabSolution®, along with the associated GAMP categorization, was reviewed. OQ of LabSolution was reviewed. The SOP for good chromatographic practices and the form for manual integration were also checked. Verification of the audit trail was regularly performed.

5. Documentation and records

Documentation system and specifications

The company used a paper-based documentation system. The structure of the documentation system at the site was guided by the integrated management system manual. The SOP for document issuance, control, archival, and destruction was reviewed. The SOP on SOP and the SOP on the document numbering system were also checked. The mentioned SOPs guided the issuance, approval, control, review, and withdrawal of procedures and quality documents. SOPs had to be reviewed every three years, unless otherwise required. Material and product specifications were detailed in written form. Similarly, analytical methods for each material and product were documented.

Equipment cleaning and use of records
Logbooks documenting equipment usage and cleaning were maintained. Several logbooks were spot-checked during the inspection, including during the site tour.

Master production and control records
Master batch production and control records were in place. The following relevant documents were briefly spot-checked:

1. Batch production record of Tenofovir disoproxil fumarate (WHO)
2. Analytical data sheet for Tenofovir disoproxil fumarate
3. Commercial batch packing record
4. Batch production record of Dolutegravir sodium (finished API)
5. Batch production record of Dolutegravir sodium (API intermediate)
6. Batch production record of Bedaquiline NBLAA salt (intermediate)
7. Batch production record of Emtricitabine (intermediate)
8. Batch production record of Lamivudine (intermediate)
9. Batch production record of Emtricitabine (finished API)

The BPRs, the analytical data sheets and the commercial batch packing records were issued and controlled as per SOP on document control.

The commercial batch packing record was common for all intermediates and finished APIs.

Batch production and control records
Production processes and quality control testing were documented in batch manufacturing and analytical records. The records properly documented the production and control processes with traceability of related activities.

Laboratory control records
Documents were generally designed, prepared, reviewed, and distributed according to a documented procedure. Laboratory control records included complete data derived from all tests conducted to ensure compliance with established specifications and standards, including examinations and assays. All raw data records and analytical reports were available; analytical reports were approved by lab management.

Batch release
The batch release process was guided by the SOP for product release. QA authorized personnel for intermediate/API release were established. Unlike the BPR review and analytical data review checklist, the review of the commercial batch packing record was not comprehensively documented, as no form was dedicated for that purpose.

Batch numbering system
The SOP for batch numbering system was in place. The SOP provided for different batch numbering of production batches (in-house) and commercial batches. In the case of reprocessing, the aforementioned SOP called for placing “RP” at the beginning of the batch number and placing “RW” in case of reworking. These two prefixes (RP and RW) were always applicable in case of production (in-house) batches. For commercial batches, marking the batch number of “RP” or “RW” applied only in case of agreement with the customer.

6. Materials management

General controls

The receipt, identification, quarantine, sampling, testing, and approval or rejection of materials were conducted according to approved documented procedures. A manual inventory system was used in all warehouses.

Sampling and testing of incoming production materials

Sampling, testing, and approval of intermediates and finished products followed the respective procedure. For each consignment, the containers were 100% sampled for identification tests, and a few containers, according to a √n+1 formula, were selected to be fully tested.

Storage

The warehouse activities were spread over one building: ground floor, Area 1: For solid and liquid incoming materials, ground floor Area 2: For finished products, and first floor: packaging materials.

Raw materials

The sampling procedure for key starting materials was reviewed. The approved supplier list for starting materials was available as a hard copy.

Supplier evaluation

Vendor qualification procedure for materials was reviewed. The SOP was applicable to all incoming material suppliers, including packaging material suppliers. The suppliers and manufacturers were audited initially before qualification, re-assessed annually by a questioner, and re-audited every 3 years within a tolerance period of 3 months. A plan for all audits to be performed in 2024 was available. The vendor qualification procedure stated that initial vendor qualification for critical raw materials may be performed in two cases. Case 1: sample performance, questionnaire evaluation, and audit. Case 2: three consecutive consignments, questionnaire, audit.

7. Production and in-process controls

In general, production operations followed defined procedures. Process flows and synthesis routes were available. Access to API plants was restricted to authorized personnel, and entry to the production suites was through change rooms.

Production operations

SOP on assigning manufacturing date for intermediate and finished products was reviewed.

Blending batches of intermediates or APIs

The SOP for operation and cleaning of the blender was reviewed. The SOP provided for blending the bulk batch (the mix of individual lots out of the vacuum tray drier [VTD]).

8. Packaging and identification labelling of APIs and intermediates

Packaging materials

Packaging operations were carried out at cleanrooms within production block II. The commercial batch packing record was common for all intermediates and finished APIs.

Label issuance and control & Packaging and labelling operations
The SOP for product release was in place and provided for issuance of labels based on customer request prior to packaging operations. The final API batch was then released after proper quality assurance checks of production and control activities.

9. Storage and distribution

Warehousing procedures
Incoming key starting materials and intermediates were quarantined after receipt until they were released for use. Upon receiving the materials, a dents verification check was performed to check for any integrity issues in the consignment. The COA was checked by QC personnel, and then the consignment was labelled and kept for quarantine until the release of the product.

Distribution procedures
Sampling and dispensing activities were controlled by QC and warehouse personnel, and the staff followed the steps from sampling procedure and dispensing procedure on sampling and dispensing of raw materials. Sampling and dispensing activities of solids and liquid materials were carried out in three separate rooms (a room for sampling solids, a room for dispensing solids, and a room for sampling and dispensing liquids without material passage). The three rooms were equipped with an airlock, and there was a space for the gowning and de-gowning of personnel. The benches for sampling and dispensing were routinely monitored for air velocity, HEPA filter leak tests, and non-viable particle monitoring every six months according to performance qualification dispensing and sampling booth warehouse. The accessories used for sampling and dispensing materials were validated for cleaning. Accessories clean hold time studies were performed according to the respective protocol.

10. Laboratory controls

The QC laboratories were separated from the production areas. They were designed and equipped with facilities for chemical and instrumental analysis, and stability studies. The laboratory had adequate space for the orderly placement of equipment and materials and for performing tests.

Receiving samples
Testing samples were received in the laboratory building. Receiving and allocation to analysts were conducted and recorded as per the respective procedure. A special sample storage area was available. Logbooks for received KSM, raw materials, IPC samples, and finished products were available and checked. The incoming samples were checked for integrity and quantity.

Testing of intermediates and APIs
The specification and testing procedure for tenofovir disoproxil fumarate was reviewed.

Validation
The analytical method validation for KSM 1-(2,2-dimethoxyethyl)-5-methoxy-6-(methoxycarbonyl)-4-oxo-1,4-dihydro pyridine-3-carboxylic acid (DTI-I) of Dolutegravir Sodium was reviewed. Glassware cleaning and validation were performed according to the procedure for handling glassware.

The procedure for analytical method transfer for intermediates and APIs was reviewed. If the method was to be transferred to an external laboratory, direct and indirect method transfer (comparing the results) and full validation had to be performed.

Qualification of analytical instruments, calibration, and verification
Most laboratory equipment was linked with Lab Solution software, with some standalone instruments such as UV and IR. Information was saved on a separate laboratory server on a daily basis and then transferred to an external hard disc on a monthly basis.

The calibration of the analytical weighting balance was assessed. Daily weight checks were performed in-house for high and low weights, with calibration conducted internally every 6 months for accuracy, reproducibility, and minimal weight. The weights used for daily checks were standardized by an external contractor, and the corresponding calibration certificates were verified. The validation report for HPLC was reviewed and discussed. LAF performance qualification was tested yearly for air velocity, HEPA filter integration, particle count test, recovery test and airflow pattern.

User privileges were checked and discussed.

Stability studies
The stability study report for Dolutegravir sodium API was verified.

Expiry and retest dates
Working reference standards were used within one year and standardized against pharmacopeial standards annually. The use of reference materials was recorded. Reference material was stored at 2–8 °C. The expiration date for pharmacopeial reference standards was checked online.

OOS Handling
The procedure for OOS investigations applicable to physical, chemical, and instrumentation testing, was briefly discussed. An initial investigation for OOS was performed to identify any laboratory errors. A hypothesis-testing investigation was used.

Retention samples.
Retention samples were stored in a separate area on the second floor of the laboratory building. Sufficient samples were retained to allow three full analyses. Retention samples were stored in the same packaging materials as for commercial use. The retained samples were inspected visually on an annual basis.

Microbiology laboratory
All microbiological testing was contracted out to external laboratories. The quality agreement with a service provider was reviewed.

11. Validation
Validation policy
The validation policy was guided by several documentations, including master validation policy and validation master plan. The VMP provided high-level guidance on different validation and qualification activities including, among others, definitions, general concepts, validation documentation, validation types, process validation (PV), cleaning validation (CV), analytical method validation (AMV) and computerized systems validation (CSV). Both mentioned documents, the master validation policy and VMP, provided for two types of re-validation: (a) re-validation in cases of known change and (b) periodic re-validation. VMP was mandated to be updated every three years. The master validation was provided

for the annual validation planner schedule. The planner schedules for 2023 and 2024 were reviewed, and some validation/qualification activities were spot-checked.

Process Validation (PV)

Procedure for process validation was in place. The procedure guided the process validation (PV) activities in terms of process design, process qualification, and continued process verification (CPV), along with prerequisites for PV, raw materials qualification, and PV documentation. The mentioned procedure provided for CPV every 6 months with at least 30 months. Policy on process re-validation was also provided in the SOP, and it was required to be performed in case of major material, process, equipment, or product change or as recommended within the CPV or PQR reports.

The validation protocols and reports of the following production processes, along with the relevant Batch production record (BPR) of the executed PV batches, were reviewed:

- PV protocol of Tenofovir Disoproxil Fumarate stage-I (TDF-I)
- PV report of Tenofovir Disoproxil Fumarate stage-I (TDF-I)
- PV report of Dolutegravir sodium (DRS-IV) [finished API]
- PV report of Dolutegravir sodium (DRS-III) [intermediate]
- PV report of Emtricitabine intermediate (FCC) [intermediate]
- PV report of Emtricitabine intermediate (ETN) [finished API]
- PV report of Lamivudine (CHE) [intermediate API]
- PV report of Bedaquiline (BQL) [intermediate API]

Cleaning Validation

The procedure for cleaning validation was in place. For the purpose of setting the limits and acceptance criteria for the efficiency of cleaning processes between different finished API products, the procedure provided calculation of maximum allowable carry-over (MACO) based on the therapeutic daily dose (TDD) of the previous product, considering permissible daily exposure (PDE) or NMT 10 ppm, whichever was less. The procedure provided for periodic re-validation of the cleaning processes every three years apart from re-validation in association with major changes in the product, process, or equipment.

The following CV protocols and reports were reviewed:

- Protocol for CV of TDF-I
- Report for CV of TDF-I
- Assessment of MACO for permissible daily exposure (PDE) of TDF-I
- Report for CV of DRS-IV
- Protocol for CV of EMC-I
- Report for CV of DRS-IV
- PDE determination strategies for DRS-IV, EMC-I and TDF-I including qualification of the toxicologist.

12. Change control

SOP for change control was reviewed and example changes were spot-checked.

13. Rejection and re-use of materials

Reprocessing and Reworking

SOP for reprocessing and reworking of intermediates and API's was in place.

Recovery of materials and solvents

SOP for handling and storage of recovery of solvent and recovery materials was in place.

14. Complaints and recalls

Product complaints followed the principles described in the respective procedure. Complaints were categorized into three levels depending on criticality, with specified timeline requirements for completion. Recalls classified as critical should be closed within 10 days, major within 30 days, and minor within 45 days. A total of five complaints were recorded for the year 2023. Example complaints were checked and discussed.

The product recall followed the principles described in the respective procedure. The recalls were to be completed within 7 days from the date of recall imitation. The SOP provided appropriate instructions to recall or remove products from the market. No recalls have been initiated for the year 2023. Mock recalls were performed every 3 years if no actual recalls were performed in these years. The recall reports was reviewed.

15. Contract manufacturers (including laboratories)

Quality agreements were spot-checked. Contracts permitted the contract giver to audit the contract acceptor's facilities for compliance with GMP. The contract acceptor and contract giver's responsibilities were clearly defined. External contract laboratory testing was used for a limited number of specialist analytical procedures; they contracted with 12 external laboratories.

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, ***Styrax Pharma Pvt Ltd***, located at ***Plot No. 27B, Jawaharlal Nehru Pharma City, Parawada, Anakapalli Andhra Pradesh 531021 India*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines for APIs.

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

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

Part 4	List of GMP guidelines referenced in the inspection report

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

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

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

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

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

6. WHO good practices for pharmaceutical quality control laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1.
   Short name: WHO TRS No. 957, Annex 1
   https://www.who.int/publications/m/item/trs957-annex1

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
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