20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

WHO PUBLIC INSPECTION REPORT

(WHOPIR)

Finished Product Manufacturer

Part 1: General information

Name of Manufacturer	Shasun Pharmaceuticals Limited
Unit number	Unit II-Formulations
Production Block	NA
Physical address	R.S. No. 32-34, PIMS Road, Periyakalapet, Puducherry, India 605 014
Contact address.	Mr. Devendra Patel, pateldevendra@stridesshasun.com
Date of inspection	23 – 25 April 2015
Type of inspection	Routine inspection
Dosage forms(s) included in the inspection	Immediate release film coated tablets and dispersible tablets and Hard capsules
WHO product numbers covered by the inspection	1 TB306: Cycloserine Capsules, hard 250mg 2 HA426: Lamivudine/Nevirapine/Zidovudine Tablet 150/200/300mg 3 HA433: Lamivudine/Nevirapine/Zidovudine Dispersible Tablet 30/50/60mg 4 HA551: Emtricitabine /Tenofovir Disoproxil Fumarate 200/300mg Tablet 5 HA525: Lamivudine / Tenofovir disoproxil Fumarate 300/300mg Tablet 6 HA527: Efavirenz / Emtricitabine / Tenofovir Disoproxil Fumarate 600/200/300mg Tablet 7 HA323: Lamivudine/Nevirapine/Zidovudine Tablet 150/200/300mg
Summary of the activities performed by the manufacturer	Manufacture, packing, testing and release of solid oral dosage for in form of tablets and hard gelatine capsules

Part 2: Summary

General information about the company and site

Shasun Pharmaceuticals Limited was incorporated in 1976. The site inspected is located in R.S. No. 32-34, PIMS Road, Periyakalapet, Puducherry, India 605 014. The site manufactures Non-sterile OSDs including tablets and hard capsules. The total area of the site is 650,000 sq. ft. The number of personnel at the time of the inspection was approximately 645.

The company has other manufacturing sites in India as below:

1. Ibuprofen API Facility, Puducherry
2. Biotech Facility, Puducherry
3. Multi-Product API Facility, Cuddalore

History of WHO and/or regulatory agency inspections

This was the second WHO inspection with previous inspections by the WHO performed on 13-16 March 2012. The site had been inspected by US FDA in 2013 and 2015, MHRA in 2010 and 2013.

Focus of the inspection

The inspection focused on the production and control of hard capsules and tablet products listed in the inspection scope. The inspection covered most of the sections of the WHO GMP text, including premises, equipment, documentation, materials, validation, sanitation and hygiene, production, quality control and utilities.

Inspected Areas

- Quality Assurance
- Sanitization and hygiene
- Qualification and validation
- Complaints
- Recalls
- Self-inspection
- Personnel
- Training
- Personal hygiene
- Premises
- Equipment
- Materials
- Documentation
- Production
- Quality control

2.1 PHARMACEUTICAL QUALITY SYSTEM

Quality risk management

The procedure for risk management was in place and it was stated that it had been applied in various areas including validation, change control and management of deviations but the procedure and risk management reports were not reviewed during this inspection.

Product quality review

Product Quality review was conducted based on a corporate procedure. The responsibility was assigned to QA. Trending using control charts was only done if there were more than a specified number of batches. There was no review of products under review by authorities or those approved but not yet commercialised.

The PQRs for the following products were reviewed:

1. **HA426 (Lamivudine/Nevirapine/Zidovudine 150/200/300mg Tablet)** for a period January to December 2014 manufactured on contract for Mylan.
2. **HA525: Lamivudine/Tenofovir Disoproxil Fumarate 300/300mg Tablet** manufactured on contract for Ranbaxy.
3. **HA433: Lamivudine/Nevirapine/Zidovudine Dispersible Tablet 30/50/60mg,** only 6 batches had so far been manufactured, 3 in 2013 and 3 in 2014.

Change control:

In 2014, there were several hundred of changes across all products. One change initiated in February 2014 in the standard testing procedure for Zidovudine and Nevirapine was reviewed. Non-compliances observed during the inspection that were listed in the full report regarding the implementation and documentation of the change control process were addressed by the manufacturer to a satisfactory level.

2.2 GOOD MANUFACTURING PRACTICES FOR PHARMACEUTICAL PRODUCTS

Good manufacturing practices generally were implemented. Necessary resources were provided, including qualified and trained personnel, adequate premises, suitable equipment and services, appropriate materials, containers, approved procedures and instructions, laboratories and equipment for in-process and other controls. Qualification and validation were performed. Manufacturing steps were recorded in batch manufacturing and packaging records. Manufacturing processes were defined and reviewed. Product was released by the authorized persons.

2.3 SANITATION AND HYGIENE

In general, premises and equipment were maintained at a satisfactory level of cleanliness. The company had a standard operating procedure as the basis for its approach to personal hygiene and sanitation in its production facility.

2.4 QUALIFICATION AND VALIDATION

Validation policy
The company's overall validation policy was described in a Validation Master Plan and SOP for Process Validation. The company identified what qualification and validation work was required.

Qualification
Since the last WHO inspection the company had installed SAP system for material management. Qualification of the SAP system was not reviewed during the inspection but the team did a spot check.

Process validation
TB306 Cycloserine hard capsules 250mg: process validation protocol and report were reviewed. Non-compliances observed during the inspection that were listed in the full report regarding the implementation and documentation of the change control process were addressed by the manufacturer to a satisfactory level.

Cleaning validation
Cleaning validation was performed according to a SOP for Cleaning Validation Programme. A matrix was available to show the worst case of maximum acceptable carry over residues (MACO). The cleaning validation report for a blender was reviewed and considered acceptable.

2.5 COMPLAINTS
Complaints were handled according to a SOP. Complaint log book for 2015 was available for review. The complaints investigation and management regarding the mix-up and regarding the external object in the tablet were reviewed and found acceptable.

2.6 PRODUCT RECALLS
A SOP described the procedure for handling recalls. The recall was classified into four classes. The inspected products were manufactured on contact for other companies except the Cycloserine capsules.

2.7 CONTRACT PRODUCTION AND ANALYSIS
Production operations were not contracted out. Some analytical tests were contracted out to contract laboratories. This was not covered by this inspection due to the time constrained.

2.8 SELF INSPECTION AND QUALITY AUDIT
Self-inspection was not covered by this inspection.

Quality audit and Supplier's approval
Company had valid written technical agreements with its suppliers and had procedures in place for evaluating and approving them, which included the use of questionnaires, site audits and lab testing of samples. Non-compliances observed during the inspection that were listed in the full report regarding the vendor approval were addressed by the manufacturer to a satisfactory level.

Suppliers were classified as either provisional or approved and the company accepted "certificates of declaration" from contract givers on behalf of their Provisional suppliers.

2.9 PERSONNEL

The manufacturer had an adequate number of personnel with the necessary qualifications and practical experience. Responsible members of staff and their specific duties were recorded in written job descriptions. An organization chart was available.

Job descriptions for key staff QA, QC manager and production head were reviewed and they were generally considered to be satisfactory.

2.10 TRAINING

Personnel's training was conducted according to a SOP. Members of Staff were required to undergo induction training and on job training. Detailed specific training required for analyst qualification was considered to be appropriate.

Requirements for ongoing training were included in the SOP and there was Training Plan for 2015. Training effectiveness was required to be evaluated. Assessment was by questionnaire and/or written test.

2.11 PERSONAL HYGIENE

The necessary requirements were fulfilled. Full gowning was in use in the grade D production areas. All changing rooms were provided with SOPs with clear photographs which pictorially described the gowning procedures. The approach to sanitation and hygiene was acceptable in general. Non-compliances observed during the inspection that were listed in the full report regarding hand washing were addressed by the manufacturer to a satisfactory level.

2.12 PREMISES

Manufacturing areas and the QC laboratory were generally of a good standard. Pressure differentials between each zone and manufacturing rooms were monitored. Non-compliances observed during the inspection that were listed in the full report regarding Premises and a risk of potential cross contamination were addressed by the manufacturer to an acceptable level and should be verified in future inspections.

2.13 EQUIPMENT

Equipment was generally of a good standard, clean and well maintained. Equipment was not dedicated in general.

2.14 MATERIALS

Material management was reviewed. The company indicated that SAP was the main system used for material and inventory control, and in actual practice, this was maintained in parallel with a paper based system. Non-compliances observed during the inspection that were listed in the full report regarding the material management in the SAP system were addressed by the manufacturer to a satisfactory level.

2.15 DOCUMENTATION

Document control was generally effective as Company had an approved procedure for control of documents.

2.16 GOOD PRACTICES IN PRODUCTION

Cycloserine capsules were not being manufactured at the time of the inspection and there were no other activities in most of the areas used for this product.

Material dispensing was performed in an area equipped with a LAF booth. Powders were mixed in a blender and unloaded into container that could then be inverted on the encapsulation machine as a hopper. A common room for in-process controls was available and suitable equipment was available. The packaging area included suitable protection for exposed product and segregation between packaging lines.

The manufacturing of the other tablets was in process at different stage at the time of inspection.

2.17 GOOD PRACTICES IN QUALITY CONTROL

Starting materials were sampled and tested. Some materials received were checked for identity using NIR.

Approved specifications and reference specimens were available.

Out of specifications (OOS) test results were handled according to a SOP. The procedure was reviewed and discussed. Non-compliances observed during the inspection that were listed in the full report regarding the OOS investigation procedure were addressed by the manufacturer to a satisfactory level.

The specifications, HPLC test method for assay, worksheets, test records and equipment maintenance were available for inspection. Tests followed the instructions given in the relevant written test procedure.

The QC laboratory visit also included an inspection of reference substances, stability studies and data integrity.

Part 3: Conclusion

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, as well as the corrective actions taken and planned, Formulation Unit II, Shasun Pharmaceuticals Ltd, located at R.S. No. 32-34, PIMS Road, Periyakalapet, Pondicherry, India 605 014 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.