TMDA/DMC/MCIE/F/001

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

TMDA
Tanzania Medicines & Medical Devices Authority

AUROBINDO PHARMA LTD UNIT-XVI, TELANGANA, INDIA
PUBLIC GMP INSPECTION REPORT

Date: 8th December, 2020

Part 1: General information about the company

Manufacturers details	
Name of manufacturer	Aurobindo Pharma Ltd, Unit -XVI
Corporate address of manufacturer	Mark building Plot No. 11, survey No. 9, Hitech City, Kondapur, Hyderabad, Telangana Code: 500084, Tel: +91 4023736370.
Inspected site	
Name & address of inspected manufacturing site	Plot No. S-5/B, S-6 &S-7, Survey No. 408-412, 418-435, 437-445, 452-459, TSIIC, SEZ, Polepally village, Jadcherla mandal, mahaboob Nagar, Telangana, **India.**
Unit	Unit –XVI
Inspection details	
Date of inspection	18th - 19th April 2019
Type of inspection	Pre-registration inspection
Introduction	
General information about the company and site	Aurobindo Pharma Limited, Unit-XVI is located plot No. 11 survey No.9 Hitech city, Kondapur, approximately 2km on the National Highway from Hyderabad to Bangalore (NH – 7). The site had a licence number 07/MN/TS/2016/F/G, dated 14th March, 2016 valid up to 13th March, 2021 issued by the Drugs Control Administration, State Government of Telangana. The site was manufacturing beta lactam dry powder for injection and lyophilized cake for injection.
History	The facility had been inspected and approved by the Drugs Control Administration of Telangana The facility had also been inspected and approved by other NMRAs including USFDA and ANVISA (Brazil)
Brief report of the activities undertaken	
Areas inspected	External surroundings, raw material receiving area, raw material and packaging materials warehouses, production areas, packing area, finished goods store, quality control laboratory and utilities
Restrictions	Inspection focused on products for which application for registration had been submitted to TMDA
Out of Scope	Production lines for which application for product

	registration had not been submitted
Production lines inspected by TMDA	Beta lactam (Penicillin) dry powder injectable line
Abbreviations	**Meaning**
AHU	Air Handling Unit
DG	Diesel Generator
EHS	Environment, Health and Safety
GMP	Good manufacturing Practice
HEPA	High Efficiency Particulate Air
OHC	Occupational Health Centre
PPGI	Repainted Galvanized Steel
QC	Quality Control
TMDA	Tanzania Medicines and Medical Devices Authority
SOP	Standard Operating Procedure

Part 2 Brief summary of the findings and comments

1. Personnel

The company had sufficient number of personnel with key posts occupied by full time qualified and experienced persons. The key personnel were provided with job description. Production and quality control sections were independent of each other as indicated in the organization chart. Training programme and schedules for all employees which were approved by respective heads were available. New employees received specific and continuous refresher training on GMP.

Requirements for personnel hygiene and medical checkup were described in the standard operating procedure. Medical examination was performed once before employment, vision checkup was done after every six (6) months and periodic medical checkup was done annually.

2. Premises

There were three buildings/blocks in the compound namely manufacturing, Utility and Administration. The manufacturing block housed production, warehouse, Quality Assurance, Quality Control Laboratory and Microbiology Laboratory.

The utility building comprised of DG set, compressed air, water treatment system, engineering and electrical panel. The Administration block housed human resources, administration, security office, OHC and EHS Department.

2.1. Layout and Design

The layout and design of the building provided separate entries for personnel and materials and unidirectional flow of manufacturing activities and materials.

The walls and ceiling of all the supporting areas including change rooms were with PPGI sandwich panels. All the corners were suitably covered with aluminium covings to ease cleaning to avoid dust and dirt accumulation.

There was epoxy flooring for the entire processing areas. In raw materials and packaging material store, all walls and ceilings were with synthetic sandwich panels with vinyl flooring.

All the ceilings had smooth finish. All the ceiling fixtures such as light fittings, air outlets and returns were designed to assure easy cleaning and to minimize the potential for accumulation of dust. All utilities entered processing areas through a closed system and the user points were designed to minimize dust accumulation and to facilitate cleaning.

2.2. Sanitation and Hygiene

The production areas were provided with airlocks for personnel and material entries, air shower in some places and cabinets for storage of garments. The change rooms were provided with hand sanitizers. Gowning procedures and pictorial presentation for access to the classified area through cross over benches were in place. All workers were provided with appropriate clean factory gowns and protective gears. The cleaning of the premises and equipment was done in accordance with the existing standard operating procedures (SOPs).

The buildings were maintained to prevent entry of insects, pests, birds, vermin and rodents. Pests and rodents control was done as per standard operating procedure (SOP).

3. Production

The manufacturing block had one dry powder for injection and two Lyophilized injectable lines which were in operation. The inspection covered the dry powder for injection line only

There were rooms for storage of raw materials, packaging materials and finished products. Storage conditions were properly maintained. Temperature and relative humidity were monitored through Building Management System and records were maintained.

Sampling of starting materials was done as per standard operating procedure (SOP). In storage areas, quarantined, under test and approved materials were clearly identified by use of a computerized system. Printed labels were secured under lock and key.

Dispensing of raw materials took place under controlled environment under laminar flow. Environmental monitoring of the area was carried out as per SOP. Filling took place under zone A surrounded by zone B. Operators were well trained and adhered to

all requirements while filling process was on going. Environmental monitoring was performed as per SOP during filling and on regular basis as per schedule.

4. Quality Control

Quality control laboratory consisted of chemical, instrumentation and microbiology sections. The laboratory was used for testing of raw materials, packaging materials, in-process and finished products. The laboratory was sufficiently equipped and the respective instruments and equipment were calibrated and/or qualified in accordance with standard operating procedures (SOPs).

In the chemistry section, volumetric solutions and working standards were prepared, stored, standardized and handled as per procedure. Tests were performed according to written procedures and recorded accordingly. There was traceability of activities and records.

Microbiology section was designed to have separate areas for conducting sterility tests, Bacterial Endotoxin Tests (BET) and bioburden tests, culture handling, incubation and decontamination. All cultures were handled under the biosafety cabinet for the purpose of protecting the analyst, environment and products.

5. Equipment

The facility had sufficient number of production equipment which were designed, installed, qualified and maintained to suit the operations carried out. The design and location of equipment also facilitated effective cleaning and avoided chances of contamination and cross contamination.

6. Water Treatment System

The facility used chlorinated bore well water as feed water for generation of purified water. Purified water was then used as feed water for generation of water for injection through two multi- distillation columns. Purified water was generated through double Reverse Osmosis, Electro Deionization (EDI) and ultrafiltration and it was required to meet USP/Ph. Eur specifications.

Purified water samples from user/sampling points were tested by quality control as per schedule and standard operating procedure (SOP). The distribution supply lines of purified water and water for injection were made of stainless steel (SS 316L) materials with internal electro-polishing. Purified water was maintained in circulation at ambient temperature while water for injection was maintained at a temperature of not less than 80^0C during storage, distribution and at the return loop.

Distribution of purified water was through an online conductivity sensor and transmitter positioned in a continuous recirculation loop to various user points in production, microbiology, quality control and warehouse through UV sterilizer.

7. Heating, Ventilation and Air Conditioning

AHUs catering to critical areas such as filling/sealing of vials were provided with Plenum and Terminal HEPA filters, while AHUs catering to lesser critical areas such as washing area for vials, air was filtered through 10 microns, 5 microns and 0.3 microns terminal HEPA. The HEPA filters had 99.99% efficiency.

The areas catered by air handling units were maintained at a temperature not exceeding 25°C and relative humidity not exceeding 55%. Wherever required, based on the product requirement, lower Relative Humidity could be maintained. The differential pressure controls between two different classes were maintained at a pressure of not less than 10 Pascals.

Dedicated room for filters cleaning was available. Filters were cleaned through a cycle involving compressed air and water and dried using compressed air.

8. Document Review

A documentation system was in place to guide production and control of products. These included updated Site Master File, Validation Master Plan (VMP); Standard Operating Procedures; qualification and validation protocols, and reports.

There were corresponding records in form of reports, forms, checklists, logbooks, registers maintained as evidence of compliance with the procedures and specifications.

Part 3 Conclusion

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, **Aurobindo Pharma Limited, Unit-XVI, Plot No. S-5/B, S-6 &S-7, Survey No. 408-412, 418-435, 437-445, 452-459, TSIIC, SEZ, Polepally village, Jadcherla mandal, mahaboob Nagar, India,** was considered to be operating at an acceptable level of compliance with the East African GMP Guidelines for the production of beta-lactam (Penicillin) dry powder injections.

This TPIR will remain valid for 3 years from the date of approval for GMP compliance provided that the outcome of any inspection conducted during this period is positive.

Part 4 References

1. TFDA, (2008), *Good manufacturing practices guidelines for pharmaceutical*, Tanzania medicines and medical devices Authority, Dar-es Salaam, Tanzania.
2. Compendium of Good Manufacturing Practices (GMP) Technical Documents for Harmonization of Medicines Regulation in the East African Community, Version: September 2014
3. TMDA Good manufacturing practices manual and SOPs, Tanzania Food and Drugs Authority, Dar-es-Salaam, Tanzania.
4. Tanzania Medicines and Medical Devices Act, Cap 219.
5. Aurobindo Pharma Limited, Unit XVI Inspection Report April, 2019.