TMDA/DMC/MCIE/F/001

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

TMDA
Tanzania Medicines & Medical Devices Authority

NATCO PHARMA LIMITED-TELANGANA, INDIA
PUBLIC GMP INSPECTION REPORT

November, 2022

Part 1: General information about the company

Manufacturers details	
Name of manufacturer	Natco Pharma Limited
Corporate address of manufacturer	Natco Pharma Limited, Road no.02, Banjara Hills, Hyderabard 500034, Telangana, **India**
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Natco Pharma Limited, Parenteral Division, Hill colony, Nagarjuna sagar, Telangana 508202, **India**
Unit/ block/ workshop number	N/A
Inspection details	
Date of inspection	15-16th November, 2019
Type of inspection	Pre registration GMP inspection
Introduction	
General information about the company and site	Natco Pharma Limited was located adjacent to the river banks of Krishna, 150KM away from Hyderabard The facility was involved in manufacturing and packaging of Liquid injection comprising of small and large volume, Lyophilized products, Sterile dry powder (Beta lactam injectable) and oncology products
History	Natco Pharma Limited is among the Natco group of Companies which was incorporated in 1981 actively engaged in developing, manufacturing and marketing (both domestic and export) comprehensive range of pharmaceutical formulation This was the pre registration GMP inspection upon submission of the application for Marketing Authorization of their products in Tanzania The facility had been issued a licence by Drug Control Administration (DCA) of Telangana to manufacture and pack various formulations of liquid injection comprising of small and large volume, Lyophilized products, Sterile dry powder

	(Beta lactam injectable) and oncology products The facility had also been inspected and approved by NMRAs of Ethiopia and Uganda
Brief report of the activities undertaken	
Areas inspected	External surrounding, Utilities, Materials receiving area, Incoming materials and Finished goods warehouses, Production areas and Quality Control Laboratories The inspection also covered the following areas; personnel, premises layout and design, sanitation, state of the buildings, equipments used in various manufacturing operations and documentation system
Restrictions	The inspection focused on production lines for products applied for marketing authorization in Tanzania
Out of scope	Lines for which application for product registration had not been submitted to TMDA
Production lines inspected by TMDA	Manufacturing and packaging lines for; • general pharmaceuticals in form of lyophilized products, small and large volume parenteral; • beta lactam injectable in form of dry powder for injection; and • oncology products
Abbreviations	**Meaning**
AHU	Air Handling Unit
BN	Batch number
BOD	Biological Oxygen Demand
BMS	Building Monitoring System
EAC	East African Community
ETP	Effluent Treatment Plant
GMP	Good Manufacturing Practice
HEPA	High Efficiency Particulate Air
HVAC	Heating, Ventilation and Air conditioning
HPLC	High Performance Liquid Chromatography
LVP	Large Volume Parenteral
SOP	Standard Operating Procedure
SVP	Small Volume Parenteral
PFW	Purified Water
TOC	Total Organic Carbon
TMDA	Tanzania Medicines and Medical Devices
RLAF	Reverse Laminar Air Flow
RCC	Reinforced Cement Concrete
WFI	Water For Injection

Part 2: Brief summary of the findings and comments

1. Personnel

The facility had adequate number of personnel to carry out manufacturing and quality control activities and the same had requisite qualification and experience. There was a key personnel for Quality assurance, production and quality control.

It was confirmed that positions for key personnel were occupied by permanent employed, qualified and experienced staffs. Review of Organization chart and job descriptions of key personnel showed that Quality control functions were independent and separated from production.

Medical examination policy was in place and that all employees were medically examined prior to employment and on yearly bases after employment. Training procedures were stipulated on SOP/QA082/F01 where by employees received induction training during recruitment and continuous trainings after recruitment.

2. Premises

i. Layout and Design

The facility consisted of three (3) manufacturing blocks and other independent blocks for administration, engineering and utilities. External walls were constructed with reinforced cement concrete (RCC) and inner partitions constructed with powder coated modular wall panels with false ceiling. Interior surfaces (walls, floors and ceilings) were smooth and free from cracks to avoid dust accumulation and permit easy cleaning and disinfection.

The manufacturing blocks for general liquid, lyophilized and dry powder for injection were designed to allow materials to flow in one direction and in a manner to prevent mix ups and cross contamination with enough space to suit operations carried out.

ii. Sanitation and Hygiene

External surroundings of the facility were tidy, maintained and clean enough to reduce dust and contaminants. Outer walls were well painted and there were no patches observed. Scrap yard was provided at appropriate location and was clearly maintained, rodent catchers were available to prevent pests and rodent entrance.

General hygiene was practiced as personnel were observed properly dressed with neat and clean factory gowns, gloves and masks as safety gears were applicable.

There were pictorial illustrations for procedures for changing gowns at each changing room and the same was observed to be adhered. Distinct color code dresses were used to identify personnel working at each manufacturing block.

There were controlled procedures for materials and personnel entry into the warehouse and at each manufacturing block. De-dusting of the incoming materials was done by using a vacuum

cleaner. Changing rooms were provided for personnel and each changing room was equipped with lockers, step over benches, hand washers, air blowers and disinfectants.

Effluent treatment plant was available to ensure treatment and safe disposal of effluent water generated from manufacturing and washing operations.

3. Production

i. Production Line I (GI Block)

GI block produced small and large volume liquid and lyophilized injection. It had three (3) production lines at ground floor; SVP line, LVP line and vials line. Production activities at all lines were supervised by qualified and experienced personnel.

Adequate equipment and facilities were available to enable production activities. Manufacturing processes involved dispensing, bottle washing and depyrogenation, aseptic filling and sealing under vertical laminar flow work station. Final product was subjected to terminal sterilization and in case of lyophilized injection to lyophilization process before visual inspection.

In process quality checks for pH, appearance, sterility and fill volume were performed at appropriate stages as per procedure.

ii. Production Line II (SDP Block)

Sterile materials from warehouse were transferred to production areas through materials pass box and undergo mixing process. Visually inspected vials and stoppers were washed and dehydrogenated, seals were sanitized and dried. Vial washing, depyrogenation and drying was followed by vial filling, stoppering and sealing, inspection and final packing of the finished product.

Throughout manufacturing processes, rooms and equipment had status label to indicate activities. Environmental monitoring was performed and settle plates were found placed various locations in the manufacturing areas, records maintained.

iii. Production at Cyto Block

There was a separate facility for the manufacturing of oncology products. The manufacturing process for oncology products involved vial washing, sterilization, filling and sealing. This inspection verified that manufacturing processes were conducted as per procedure and the same was found adequate.

4. Quality Control

Quality control laboratory was separated into instrument room, wet chemistry, microbiology, stability testing and sample retention room. All sections in quality control laboratory were adequately equipped, properly arranged with enough space to permit activities to be carried out.

Personnel with appropriate qualification and experience were employed and proficiency testing was conducted as per schedule. Instruments were periodically calibrated and validated through

documented standard calibration procedures as per schedule. Reference standards and working standards were stored under lock and key.

Stability studies were performed depending on the zones where the product will be marketed and as such three (3) batches submitted for Zoledronic acid infusion registration in Tanzania were found still under stability studies as incomplete results were submitted during dossier assessment.

The sample retention room was clean, well arranged, labeled and had enough space with temperature and humidity monitoring devices and their records and procedure for tracing samples was verified and found adequate.

5. Equipment

The facility had a sufficient number of equipment for production and quality control which were designed, located, installed, calibrated and/or qualified and maintained to suit the operations carried out.

Equipment design facilitated effective cleaning to prevent chances of contamination and cross contamination.

6. Purified water System

The facility sourced water from river Krishna which then underwent chlorination, sand filtration and carbon filtration before being stored in a stainless steel tank (2000 litres). Water distribution pipe lines and storage tanks were of stainless steel 316 L grade.

Purification system was done by passing through 10µ filters, activated carbon column, cation resin column, anion resin column, mixed bed resin column and particle retention filter (5µ) to produce DI water. DI water fed the WFI generation plant where it was further treated by UV sanitization, mixed bed resin column, filtration and ultra-filtration.

Direction flow arrows and schematic drawing of the water system operation were available and accepted. Conductivity and schedule for sampling were recorded in a logbook and the same was reviewed and found adequate.

Sampling points were labeled and records for testing of water were found. Qualification records of the system were also verified and found acceptable

7. Heating, Ventilation and Air Conditioning

Heating, ventilation and air conditioning system was installed at each manufacturing block to supply filtered air and maintain adequate temperature, pressure differential and relative humidity at all core production areas. A total of 25 AHUs were installed to supply air to the facility.

Air supply involved 90% re-circulated air from the operational areas and 10% fresh air. The AHUs that supplied air to critical areas were provided with terminal HEPA filters. Pressure differential of NLT 0.6 to 1.6 mm of water column was maintained. Routine preventive maintenance was done as per schedule and the same were found adequate. Temperature,

relative humidity and differential pressure across the processing rooms were centrally monitored through qualified Building Monitoring System (BMS).

8. Document Review

The facility had a proper documentation system and the documents were prepared, reviewed and approved before distribution. Preparation, checks and approval were done by the appropriate responsible personnel. Documents reviewed included updated Site Master File, Validation Master Plans (VMP); Standard Operating Procedures; standard testing procedures, qualification, validation protocols and reports among others.

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, including the observations listed in the report, **Natco Pharma Limited, Parenteral Division, Hill colony, Nagarjuna sagar, Telangana 508202, India** was considered to be operating at an acceptable level of compliance with East African community GMP Guidelines.

This TPIR will remain valid for three (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. Compendium of Good Manufacturing Practices (GMP) Technical Document for Harmonization of Medicines Regulation in the East African Community, Version: September 2014.
2. TMDA Good Manufacturing Practices Manual and SOPs, Tanzania Medicines and Medical Devices Authority, Dar es Salaam, Tanzania.
3. Narco Pharma Limited GMP Inspection report December, 2020.
4. Tanzania Medicines and Medical Devices Act, Cap 219.