TMDA/DMC/MCIE/F/001

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

(MANKIND PHARMA LIMITED UNIT I)
PUBLIC GMP INSPECTION REPORT

December, 2020

Part 1: General information about the company

Manufacturers details	
Name of manufacturer	Mankind Pharma Limited
Corporate address of manufacturer	208, Okhla Industrial Estate, Phase-3, New Delhi-110020 (INDIA)
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Village Kishanpura, P.O Jamniwala, Tehsil Paonta Sahib, District Sirmour-173025, Himachal Pradesh, India
Unit/ block/ workshop number	Unit I
Inspection details	
Date of inspection	19th – 20th December 2019
Type of inspection	Renewal inspection
Introduction	
General information about the company and site	Mankind Pharma Limited-Unit I is located in the tax free zone of Himachal Pradesh at Village Kishanpura, Paonta Sahib, District Sirmour, Himachal Pradesh, India which is approximately 260 Kilometers from New Delhi and 140 Kilometers from Chandigarh. The facility is engaged in the manufacturing of non-cephalosporin sterile small volume liquid injectables and cephalosporin dry powder injectables.
History	Mankind Pharma Limited Unit I acquired manufacturing licence No. MB/06/480 on 28th February, 2007 from the Drug Controller, Himachal Pradesh, India. The renewed licence is valid till 27th February 2022. The manufacturing site had been inspected and certified by Kenya, Ukraine, Uganda, Malaysia, Ivory Coast, Cambodia, Sri Lanka, Philippines, Nigeria and Ethiopia for small volume liquid injection and dry powder injection. It was inspected for the first time by Tanzania Medicines and Medical Devices Authority (TMDA) in 2013 and found to be GMP Compliant. This was the second renewal inspection conducted by TMDA to this facility.
Brief report of the activities undertaken	
Areas inspected	Areas inspected were external surroundings, production

	area, storage area for starting materials, packaging and finished goods, quality control laboratory and utilities. The inspection also verified the qualification of key personnel and training, premises layout, design, sanitation and hygiene, state of the buildings and equipment used in various manufacturing operations, laboratory instruments, complaints handling and recalls, self-inspection, documentation, qualification and validation as well as production and quality control practices.
Restrictions	Only the manufacturing facilities and activities pertaining to registered products and those under registration process were inspected.
Out of scope	All activities apart from the ones mentioned above were not inspected.
Production lines inspected by TMDA	Line I and II of the general ampoule block (non-cephalosporin block) and cephalosporin vial block and their packing lines
Abbreviations	**Meaning**
AHU	Air Handling Unit
EAC	East African Community
cGMP	Current Good Manufacturing Practices
HVAC	Heating, ventilation and air conditioning
PW	Purified Water
SMF	Site Master File
SOP's	Standard Operating Procedures
TMDA	Tanzania Medicines and Medical Devices Authority
WFI	Water for Injection

Part 2: Brief summary of the findings and comments

1. Personnel

Manufacturer had sufficient number of qualified and experienced personnel to carry out production, quality control and quality assurance activities. Key posts were occupied by full time personnel with clearly defined responsibilities and job descriptions. Head of Production and Head of Quality Control were independent from each other as indicated in the Company's Organization Chart.

Induction and on job trainings were provided and records indicated employees' awareness on GMP and safety principles. Personnel were subjected to medical examination as per documented procedure which involved pre-employment and annual medical examination.
Adequate personnel hygiene measures were taken such that during the inspection personnel had clean uniforms and found to observe hygienic practices.

2. Premises

i. Layout and Design

The facility was provided with all necessary areas and sections as per Good Manufacturing Practices (GMP) principles. The layout allowed for a unidirectional flow of material and personnel to prevent cross and/or contamination. Generally, the premises were suitably located, constructed and maintained to suit the operations which were carried out.

Manufacturing site had three separate buildings, line I and II general ampoule block, cephalosporin vial block (dry powder for injection) and line III general ampoule block. The blocks were designed independently in such a way that each had separate dedicated areas for warehouse, production lines and packaging areas, purified and water for injection plants, steam generation and HVAC systems.

The facility was constructed with cement and concrete slabs. Core manufacturing areas were made up of sandwich type 100 mm thick SS panels with epoxy flooring. Curving between floor and walls and between ceiling and walls were observed to facilitate effective cleanliness. The construction materials were of fire resistant and the buildings were equipped with a sprinkler system for fire protection. The corridors were designed to enhance viewing of the manufacturing operations. Electrical supply, lighting, temperature, humidity and ventilation were inspected and found in general, appropriate for manufacture and functioning of equipment.

ii. Sanitation and Hygiene

External surroundings were clean and well maintained. Suitable and validated procedures and relevant records were available for general cleaning and cleaning of equipment.

Personnel change rooms were provided with doors having interlocking mechanisms, change procedures supported by pictorial presentations, wash areas, cabinets for keeping street gowns and shoes, step over benches and sanitizing solutions. Separate change rooms for gents and ladies were provided.

Separate entry points for incoming raw material and packaging materials were provided. The receiving bays had adequate infrastructures including air curtains, air shower, de-dusting and weighing equipment and cleaning procedures. Rodents and pests' traps were provided at appropriate locations to prevent entry to production area.

3. Production

Line I and II general ampoule production block

Personnel entry to the warehouse was separate from raw material entry. Raw materials were received and stored in the raw materials stores. Receiving bay was available where de-dusting of materials was done by using a vacuum cleaner and followed by materials weight check in which a calibrated balance was available for verification of weight. The procedures for receiving raw and packaging materials as well as approved vendor list were available at the warehouse.

The space for storage of materials was observed to be adequate to allow for orderly storage of materials and cleanliness procedure was adhered. Packaging materials, printed primary packaging materials and labels were stored securely in a separate area. All incoming materials were generally controlled (quarantined, sampled, tested, released or rejected as relevant). The respective areas were provided with status labels.

Sampling and dispensing areas were also provided and were well equipped to carry out both sampling and dispensing activities. The cabinets were provided with all facilities to prevent contamination and cross-contamination which included well maintained laminar air flow, calibrated balances and magnehelic gauges. All the machines had calibration status labels. Environmental monitoring was observed to be conducted in all booths and records were maintained. The personnel responsible for sampling and dispensing were interviewed and found to be conversant with the activities they perform. The dispensed materials were observed to be taken to the production area through material pass box.

Entry of personnel to the production areas was through a series of secondary change rooms (3 change rooms). Review of Batch Manufacturing Records (BMRs) at various stages indicated that production operations were followed and documented as per written procedures.

Cephalosporin vial block

The block consisted of only one production line for dry powder injection with adequate space and storage facilities. Separate entries were available for personnel and materials entering the warehouse. The change rooms were provided with SOPs and pictorial demonstration for changing, step over benches, gowns and other protective gears and sanitizer.

In the sampling and dispensing rooms, laminar air flow cabinets were provided to prevent contamination. Entry to the production area was through a number of change rooms. Manufacturing process involved de-cartoning, vial washing, de-pyrogenation of vials, washing and sterilization of aluminum seals and rubber stoppers, blending (where required), aseptic filling (which was done under laminar air flow – class A environment), rubber stoppering, vial sealing, optical inspection, vial labeling, carton packing and final shipper packing. BMRs were checked during inspection and found complying with the requirements.

4. Quality Control

Quality control laboratory had three sections which were chemical, instrument and microbiology. Each section had sufficient number of analysts and technicians with appropriate qualifications and experience to ensure effective quality control. Adequate number of equipment designed to suit operations carried out was also available. Sufficient space was provided to minimize risk of mix-ups and sample contamination.

Tests were performed according to written procedures and appropriate records were available for traceability.

Microbiology section had dedicated areas for media preparations and decontamination. The areas were provided with incubators and bio-safety cabinets respectively. The microbiology section was carrying out microbiological analysis of raw and purified water, drug substances, finished goods and environmental monitoring. Technical support from approved analytical laboratories when deemed necessary was utilized. The responsibilities of each part were well defined in the agreement.

Control sample room was observed to be under lock and key, installed with calibrated temperature and humidity monitoring devices and samples were retained and finally disposed as per SOP. In addition, the company had a well-equipped facility to conduct stability studies.

5. Equipment

The facility had adequate number and various types of equipment and utilities. Equipment was located, designed, constructed, adapted, and maintained to suit the operations to be carried out. The layout and design of equipment minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build-up of dust or dirt.

6. Water Treatment System

The purified water systems were suitably designed, installed, validated, maintained, calibrated and monitored. The pre-treatment plant was located in the utility area outside the production block. Water was drawn from the bore well through a submersible pump and stored in overhead tank. The raw water was then chlorinated and stored in the underground tank and then passed through the multi grade filters to remove suspended solids and then de-chlorinated and transferred to the softener units. The purified water (PW) was produced by Reverse Osmosis (RO) and De ionization (DI) process which was then passed through multicolumn to produce pyrogen free water for injection (WFI).

Separate distribution systems were available for the general ampoule block and for the vial block on the first floor of each block. The system was well labeled to show direction flow, various stages and sampling points. Chemical, microbiology and endotoxins tests were carried out to monitor the quality of water as per schedule and records maintained. Cleaning and sanitization of storage and distribution system were performed as per procedures and records were found in place.

Qualification documents for the plant was also availed and it was confirmed that the system was working as expected.

7. Heating, Ventilation and Air Conditioning

The heating, ventilation and air conditioning (HVAC) system was installed in the facility to supply filtered fresh air to maintain adequate temperature and relative humidity. Dedicated re-circulating (90%) Air Handling Units (AHUs) and Ventilation and Exhaust Units have been provided for all manufacturing areas for supply of filtered air to prevent cross-contamination.

General ampoule block, Vial block and QC (microbiology) section were provided with adequate and independent air handling units (AHUs). The AHUs were qualified and the performance qualification and records were verified and found to be acceptable.

A written preventive maintenance plan for air handling units was available. The plan provides the details of maintenance activity along with frequency. The activities for maintenance of AHU include cleaning of filters, cleaning of cooling coils and drainage lines, checking and correction of drive mechanisms and leakage. Preventive maintenance of AHUs was carried out as per approved procedures.

8. Document Review

Documents were designed and prepared as per GMP requirements and distributed with care. Documents were approved, signed and dated by the appropriate responsible persons. Documents review was done in timely manner and records kept up to date.

Part 3: Conclusion

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection and assessment of compliance report, **Mankind Pharma Limited (Unit I), Village Kishanpura, P.O Jamniwala, Tehsil Paonta Sahib, District Sirmour-173025, Himachal Pradesh, India** was considered to be operating at an acceptable level of compliance with EAC GMP Guidelines for the manufacturing of sterile small volume liquid injectables (general ampoule block i.e line I & II (Non-Cephalosporin)) and sterile small volume dry powder injectables (vial block - Cephalosporin).

***This TPIR will remain valid for three (3) years from the date of approval unless the site is no longer considered to be in compliance with current GMP requirements*.**

Part 4: References

1. EAC, (2014), *Compendium of Good Manufacturing Practice Guidelines Technical Documents for Harmonization of Medicines Regulations,* EAC Secretariat, Arusha, Tanzania.

2. TMDA *Good Manufacturing Practices Regulations, Manual and SOPs*, Tanzania Medicines and Medical Devices Authority, Dar es Salaam, Tanzania.

3. Tanzania Medicines and Medical Devices Act, Cap 219.

4. Mankind Pharma Limited (Unit I) – CAPA response