TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

TMDA
Tanzania Medicines & Medical Devices Authority

PT HARSEN LABORATORIES, INDONESIA
PUBLIC GMP INSPECTION REPORT

November, 2022

Part 1: General information about the company

Manufacturers details	
Name of manufacturer	PT HARSEN LABORATORIES
Corporate address of manufacturer	PT Harsen Laboratories Jalan Raya Bogor, 24.6KM, East Jarkata, 13750, **Indonesia**
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Same as above
Unit/ block/ workshop number	NA
Inspection details	
Date of inspection	26 - 27th November, 2019
Type of inspection	Renewal GMP inspection
Introduction	
General information about the company and site	PT Harsen Laboratories is located at Jalan Raya Bogor, 24.6KM, East Jarkata, 13750, Indonesia The facility is engaged in manufacturing and packaging of general oral solid and oral liquid dosage forms, sterile small volume injections, eye drops and powder for injection (Penicillin and Cephalosporin) and , Hormones (oral solid, Liquid injection and implants). Eachprocessed in dedicated facilities
History	The facility had been registered by the National Agency for Drug and Food Control of the Republic of Indonesia (NA-FDC) and issued with a license number HK.17.IF/V/505/12 The facility was inspected and approved by other medicines regulatory authorities which include NDA (Uganda), PPB (Kenya) and NAFDAC (Nigeria). This was a GMP re-inspection after unsuccessful compliance in the previous GMP inspection
Brief report of the activities undertaken	
Areas inspected	External surroundings, utilities related to hormone

	injection manufacturing, raw materials receiving area, raw materials and packaging materials warehouses, production areas, packing area, finished goods store and quality control laboratories
Restrictions	The inspection focused on the production lines for the products registered in Tanzania
Out of scope	Lines for which application for product registration had not been submitted to TMDA
Production lines inspected by TMDA	Three (3) production lines for hormonal injections
Abbreviations	**Meaning**
AHU	Air Handling Unit
BMR	Batch Manufacturing Record
CAPA	Corrective and Preventive Action
cGMP	Current Good Manufacturing Practice
ETP	Effluent Treatment Plant
EDI	Electro de-ionization
PU	Polyurethane
HVAC	Heating, Ventilation and Air conditioning
RO	Reverse osmosis
WFI	Water for injection

Part 2: Brief summary of the findings and comments

1. Personnel

The facility was observed to have a sufficient number of personnel to handle activities relating to manufacturing and quality control. Key posts for quality assurance, quality control and production were occupied by qualified and experienced persons and they were fulltime employees. Organization chart and job description of key personnel indicated that Heads of Quality control and Production were independent.

Employees were medically examined during recruitment and on yearly bases after recruitment. It was confirmed that employees were receiving induction training during recruitment and on job trainings on cGMP, personal hygiene, sanitation and safety depending on area of work.

2. Premises

i. Layout and Design

The Hormone manufacturing building was made up of two (2) interlinking dedicated blocks for production of oral solid formulation and injectables. Each had three (3) floors in which ground floor was dedicated for packaging activities, first floor for production activities and QC and second floor for utilities (AHU and WTP).

The Hormone manufacturing plant was properly designed to allow logical flow of material and personnel. Interior surface such as walls, floors and ceiling were smooth and free from cracks to avoid accumulation of dust and permit easy cleaning and disinfection. All buildings were constructed using steel and concrete structure and cement plastered brick walls.

ii. Sanitation and Hygiene

Procedure for gowning and pictorial demonstration was in place and all employees were provided with appropriate clean factory gowns and protective gears. Changing rooms were adequate in size provided with step over benches, bins for keeping used and clean gowns, and facilities for hand washing and sanitization.

Availability of air lock, monitoring of pressure differentials, use of dedicated facilities, cleaning between campaign productions and appropriate use of air supply were measures taken to prevent possibilities of contamination and/or cross contamination at the site. Received raw and packaging materials were dedusted as per procedure before transferring to storage areas.

Pest and rodent control were done as per the company specified procedure. Generally, the external environment and buildings were clean, properly maintained and well designed to minimize risk of contamination and allow good sanitation.

3. Production

Incoming materials including packaging materials were properly received, checked, verified, weighed and cleaned in accordance with procedure. Materials were kept under quarantine before approval from QC and once approved were taken to approved section within the warehouse. Sampling and dispensing were done under LAF and had separate entry for personnel and materials. Special storage facilities were provided for sterile materials and those which required specific temperature and humidity conditions.

Production consisted of three (3) production lines for hormone injection which were provided with adequate number of equipment and instruments. The equipment and processing lines were clearly identified with status label.

Production of sterile hormones was carried out on the first floor. Manufacturing process flow involved weighing of all excipients under LAF, mixing of excipients, filtration then final mixing with sterile API, transfer of bulk preparation to filling tanks, aseptic filling in vials and rubber stoppers, capping, visual inspection, labeling and lastly secondary packaging.

All these processes were carried out in class A with B background rooms. Finished products were taken by lift to ground floor for quarantine storage waiting for Laboratory results before approval.

Environment monitoring was done as per procedure and one of the methods implemented was air sampling using settle plate to monitor bacterial contamination.

4. Quality Control

The facility had a dedicated quality control laboratory for analysis of hormonal products. The laboratory was equipped, well-arranged and had adequate space to for the activities to be carried out. It comprised of sections for instrumentation, wet chemistry, microbiology testing, stability testing and sample retention room.

Protective and safety gears including goggles, nose masks, gloves, eye wash, emergency showers, emergency doors, fume chambers and calibrated fire extinguishers were available. Reference standard and working standards were found stored in the calibrated refrigerator under lock and key.

A number of stability chambers were available with different storage condition depending on the market of the manufactured product. They included stability chambers for zone IVB climatic condition for both real time (30±2°C 75 ± 5% RH) and accelerated (40±2°C 75 ± 5% RH). Stability chambers were continuously monitored.
Sample retention room had enough space with temperature and humidity well controlled and the records were available and satisfactory.

5. Equipment

At the facility equipment were designed to facilitate effective cleaning and to prevent chances of contamination and cross contamination.

Among the available instruments were HPLC, UV/VIS spectrophotometer, Dissolution apparatus, Disintegration tester, Friability tester, Autoclaves and Reverse laminar cabinets. Instruments were considered sufficient for activities carried out. Each instrument was provided with usage manual and logbooks and upon verification of the documents were found adequate.

6. Purified water System

The facility sourced its raw water from city water and stored in a feed water tank of 1000 liters capacity. Raw water was subjected to a series of processes to obtain purified water. The processes included chlorination, sand filtration, carbon filtration, mixed bed column filtration, 5µm cartilage filters, reverse osmosis (RO 1), soft water storage tank, double reverse osmosis (RO 2), electro de-ionization (EDI) and finally collected as purified water in a SS 316L 2000 liters capacity tank. Purified water was circulated at ambient temperature in a closed loop to different user points through UV light.

Water for injection was produced by a five (5) column distillation plant and collected in SS 316L 1000 liters storage tank, distributed through SS 316L loop to user point and maintained at NLT 80°C under continuous circulation.

7. Heating, Ventilation and Air Conditioning

Heating, ventilation and air conditioning system was suitably designed and installed to maintain adequate temperature and relative humidity. The HVAC was also designed to maintain pressure differentials and supply good quality air in order to prevent contamination and/or cross contamination. Four (4) AHUs were installed to supply the injectable hormone manufacturing facility with positive pressure (NLT 5 Pa) in the processing rooms as compared to corridors which were maintained at negative pressure (NMT 15 Pa). Temperature and relative humidity were maintained between 16-25°C and 45-55% RH respectively for class A, B and C areas and between 20-27°C and NMT 60% RH for class D areas.

Each AHU was designed in such a way that 10-20% of fresh air and 80-90% of re-circulated air passed through a series of pre-filters of 10µ, 5µ and 3µ and 0.3µm before to be supplied into the manufacturing area. Filter cleaning booth was also available General design were verified and found satisfactory.

8. Document Review

A number of documents were reviewed which included manufacturing license, quality manual, organization chart, batch manufacturing records, validation master plan, protocols and reports validation, qualification reports, analytical method validation, cleaning validation. Generally, the documentation system was in place and satisfactory.

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, **PT Harsen Laboratories Jalan Raya Bogor, 24.6KM, East Jarkata, 13750, Indonesia** was considered to be operating at an acceptable level of compliance with East African Community GMP guidelines for the manufacturing of hormonal products in form of liquid injection.

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. TP Harsen Laboratories GMP Inspection report November, 2019.
4. TP Harsen Laboratories Corrective Action and Preventive Action report July, 2020
5. Tanzania Medicines and Medical Devices Act, Cap 219.