TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

TMDA
Tanzania Medicines & Medical Devices Authority

(EUGIA PHARMA SPECIALTIES LTD)
PUBLIC GMP INSPECTION REPORT

December, 2020

Part 1: General information about the company

Manufacturers details	
Name of manufacturer	Eugia Pharma Specialties Limited, Hyderabad
Corporate address of manufacturer	Plot No. 5-38, Survey No. 550, 551 & 552 Kolthur Village, Shameerpet Mandal, Medchal Malkajgir, District - Medchal, Pin 500101 Telangana State, India.
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Plot No. 5-38, Survey No. 550, 551 & 552 Kolthur Village, Shameerpet Mandal, Medchal Malkajgir, District - Medchal, Pin 500101 Telangana State, India.
Unit/ block/ workshop number	Not applicable
Inspection details	
Date of inspection	3rd – 4th October, 2018
Type of inspection	Pre – Registration GMP Inspection
Introduction	
General information about the company and site	Eugia Pharma Specialties Limited was established in September, 2013. It is located at Genome Valley, Kolthur Village, Shameerpet in Telangana state about 86.4 km from Ravij Gandhi international airport. The facility is engaged in the manufacturing of antineoplastics oral solid dosage (OSD) forms (tablets, hard gelatin capsules, soft gelatin capsules), liquid injectables (vials & pre- filled syringes (PFS) and lyophilized injectables; and hormone liquid injectables (vials and PFS) and soft gelatin capsules.
History	The facility had a GMP certificate number 24/ RR/ TS / 2015/ F/ G valid till February 2020 issued by the State Food and Drug Control Administration of Telangana, India. Hormone and Oncology production lines have been inspected and approved by USFDA in 2018.
Brief report of the activities undertaken	

Areas inspected	The pre- licensing inspection focused on the production and control of the antineoplastic and oncological products and covered all the sections of the EAC Compendium including utilities, materials, premises and equipment utilized for the manufacture and control of the products, production, quality control, sanitation and hygiene, personnel, documentation, qualification and validation.
Restriction	None
Out of scope	None
Production lines inspected by TMDA	i. Oncology: a) Oral Solid Dosage Form – tablets, hard gelatin capsules and soft gelatin capsules b) Injectables (vial and PFS) ii. Hormonal liquid injectables (vials and PFS) and tablets
Abbreviations	**Meaning**
AHU	Air Handling Unit
API	Active pharmaceutical ingredient
EAC	East African Community
GMP	Good Manufacturing Practices
HEPA	High Efficiency Particulate Air
HVAC	Heating Ventilation and Air Conditioning
QC	Quality Control
RLAF	Reverse Laminar Air Flow
RO	Reverse Osmosis
SOP	Standard Operating Procedure
SS	Stainless steel
TMDA	Tanzania Medicines and Medical Devices Authority
TPIR	TMDA Public Inspection Report
UV	Ultraviolet

Part 2: Brief Summary of findings and comments

1. Personnel

The facility had sufficient number of qualified personnel to carry out all the tasks for which the manufacturer was responsible. Review of the facility organogram and job descriptions for key personnel (head of QA, QC and Production) confirmed that they were appropriate for their assigned duties and were independent from each other in their responsibilities.

On appointment and on job training was provided to employees; interviews and records indicated that they were aware of cGMP, company policy and procedures. Personnel were subjected to medical examination prior to and during employment once in a year as per procedure. In addition, medical checkup was conducted after every six months including eye test, hormonal tests and platelet count.

2. Premises

i. Layout and Design

The premises were located, designed, constructed, adapted and maintained to suit the operations that were carried out, permit effective cleaning and minimize the risk of cross contamination. It was designed such that adequate space for orderly and logical placement of equipment and materials was provided. There were four separated blocks dedicated for hormone manufacturing, oncology manufacturing, innovation center (consisted of QC Laboratory, QA documentation office, stability chamber room and service area) and utility (engineering).

The hormone manufacturing block comprised of material warehouses, injectable manufacturing area, soft gel capsules manufacturing area, packaging area and service area. Oncology manufacturing block comprised of raw material warehouses and manufacturing areas for OSD, injectables, pre filled syringes and soft gel, packing area and the service area.

The buildings were made of ferro - concrete materials and microbiology section built up of GI powdered coated panels, painted with acryline emulsion and PU paint and further partitioned by modular panels. Ceilings in manufacturing areas were of ferro concrete, glass reinforced panel, powder coated galvanized iron or stainless steel. Floors were made up of epoxy coat with covings at all edges and angles to facilitate easy cleaning and prevent accumulation of dust or dirty.

Pipe work and light fittings were embedded to avoid creation of recesses that are difficult to clean. Windows and doors were flushed with aluminium glass in order to prevent

accumulation of dirty or dust and facilitate easy cleaning. Dedicated air handling units, reliable electrical supply and sufficient lighting were appropriate for manufacturing activities and functioning of equipment. Storage areas were spacious and well equipped to allow systematic and orderly storage of materials.

ii. Sanitation and Hygiene

Standard operating procedures for personnel hygiene, cleaning of equipment, critical and non-critical areas were in place. Separate gents and visitors change rooms were provided. Primary, secondary and tertiary dresses, shoe covers and sanitizers were provided for personnel before entering manufacturing areas, so as to minimize the particle count in clean areas. Entry and exit gowning procedures were displayed at appropriate places and were properly followed.

Cleaning in the entire production area and equipment was performed as per approved Cleaning Validation Master Plan / Protocol and methods to assure consistency and reproducibility of the procedure. Cleaning records were reviewed and found satisfactory. Rodent traps were positioned in different stations surrounding the facility to prevent rodents from entering the storage and production areas.

3. Production

There was a unidirectional flow of personnel and materials in production from where raw materials were received and stored through manufacturing operations up to finished goods store. Production areas were spacious and allowed for free movement of people and materials to avoid cross contamination. Handling of materials and products, such as receipt and cleaning, quarantine, sampling, storage, labelling, dispensing, processing, packaging, and distribution was done in accordance with written procedures, records were verified and were adequate. Printed packaging materials and labels were stored in secured areas under lock and key. During inspection production of Oral Solid Dosage (OSD) Formulations (tablets and capsules) and Liquid Injectable were in operation.

Oral Solid Dosage Formulation - Antineoplastics

Separate sampling and dispensing booths for active and inactive raw materials were provided and activities were conducted by use of isolators under reverse laminar flow cabinets. SOPs were properly maintained. Separate entrance and exit for material and personnel, airlocks and secondary change rooms with crossover benches were provided to prevent cross contamination.

Environmental monitoring for classified areas was being executed based on procedure for environmental monitoring. Records indicated that, both active (air sampler) and passive (settle plates) sampling methods were performed for sampling rooms (isolators).

Generally, the manufacturing operations were carried out according to the procedures.

Liquid Injectable – Antineoplastics

The liquid manufacturing line consisted of the compounding material area (Grade D) with the compounding isolators (Grade C). Dedicated area for sterilization of the finished product where primary and secondary filtration was done using 0.2µ filter. Moist heat sterilization was used for sterilizing the packing materials. The production area had a dedicated area for vial de-cartoning, visual inspection under RLAF and vial washing by PW, WFI and compressed air. Vial depyrogenation and sterilization was done under specified conditions and terminal sterilization at 121^0C for 60min, aseptic filling and sealing of vials in grade A surrounded by grade B area, labelling and packing was verified.

Compounding stage was monitored using the following tests; glove intergrade, pH and microbial monitoring by active and passive air sampling. While during sealing and filling, stoppering and sealing stage the following tests were monitored; microbial monitoring, online viable particle counting, RH, temperature, pressure differentials of isolators and leak test.

Oral Solid Dosage Formulation - Soft Gelatin Capsule Hormone

Dedicated sampling booths for active and inactive raw materials were provided with RLAF and separate entrance and exit for material and personnel were provided to prevent cross contamination. One common dispensing booth was provided for active materials and excipients. SOPs and records were verified and found adequate. Environmental monitoring by settle plates was performed at gelatin cooking and feed manufacturing areas as per the SOP; records were verified and were acceptable.

Generally, manufacturing processes were initiated as per the BMR; sequence of activities was followed as per procedure and properly recorded. In process control checks were performed within the production area and records maintained in BMR and BPR. Status labels were provided for each manufacturing activities for identification of each stage involved in production. The facility had packing lines for blistering and vial filling.

4. Quality Control

The facility had a quality control laboratory which was independent from other departments and under the authority of a person with appropriate qualifications and experience. It was divided into chemical analysis, instrumental analysis, and microbiology sections responsible for sampling and testing of raw materials, finished product and packaging materials. Adequate number of personnel with appropriate qualification and experience was available to ensure all activities were effectively and reliably carried out.

Separate room was provided for keeping the instruments to protect them against electrical interference, vibration, contact with external moisture and other external factors. Microbiology Lab was appropriately designed and equipped for sterility testing, bacterial endotoxin tests, microbial limit tests, culture handling, media preparation and handling and incubation of samples.

Reference and working standards were found to be stored according to storage instructions. Stability chambers were set at all temperature and humidity conditions depending on the climatic zones of the world with subsequent testing requirements. Analytical test methods were validated; validation plan / protocols and reports were verified and found adequate.

The equipments used were found to be adequate and were maintained as per respective calibration, qualification and validation procedures. Equipment log books, SOPs, calibration records and qualification reports were verified and found to be acceptable. In general, the laboratory was designed to suit the operations carried out and was provided with sufficient space to avoid mix up and cross contamination.

5. Equipment

The facility had sufficient number of production equipment which were designed, located, installed, qualified and maintained to suit the operations carried out. Equipment design facilitated effective cleaning to prevent chances of contamination and cross contamination. Cleaning, maintenance and qualification records were in place.

6. Water Treatment System

The facility had Water treatment system for pre-treatment of potable water and post treatment system for generation of purified water (PW), water for injection (WFI) and pure steam. Pre - treatment system consisted of chlorination, sand filter, softener, UF, RO-1 and storage tanks while post treatment water systems consisted of:

i. Dedicated PW generation systems for hormone and oncology blocks each comprised of RO-2, EDI, purified water SS316L storage tank, electro polished SS316L circulation loop maintained at NMT 28°C and user points.
ii. Dedicated WFI generation systems for hormone and oncology blocks each comprised of PW as feed water, multi column distillation, condenser, internal electro polished SS316L storage tank, continuous distribution loop maintained at 80 °C and user points.
iii. Dedicated pure steam generation systems for hormone and oncology block each consisting of single column distillation.

Generated water was checked regularly for their quality as per sampling plan according to documented procedures availed during inspection. Parameters monitored for PW included pH, TOC and conductivity, while WFI and pure steam was tested as per USP / EP standards. Sanitization of the WFI system was carried out at regular intervals as per standard operating procedures (SOP) while for purified water storage tank (SS 316L) was done by hot water of NLT 85^0C. Qualification documents provided evidence that the water system was designed, installed, operated and performed according to the defined specifications.

7. Heating, Ventilation and Air Conditioning

Dedicated Heating, Ventilation and Air-conditioning (HVAC) system for Hormone and Oncology blocks were installed in the facility to supply filtered fresh air and re-circulated air and maintain adequate temperature and relative humidity. AHUs were proved to function properly and supply filtered air to various dedicated manufacturing areas. Pressure differentials, temperature and humidity were also maintained within the limits as per respective area design criteria to avoid cross contamination, ensure quality of products and functioning of equipment. Monitoring of room parameters was precisely monitored by Building management system (BMS). All relevant documents to include design qualification, installation qualification, performance qualification and operational qualification were all reviewed hence proved the suitability and functionality of the system.

8. Document Review

Generally, the documentation system was functioning satisfactorily and documents were prepared, checked and approved by authorized personnel. Some of the reviewed document included Validation Master Plans (VMP); Standard Operating Procedures; Batch Manufacturing and Packaging Instructions and records; specifications of starting materials, packaging materials, packaging components, intermediates and finished products; standard testing procedures, analytical records and certificates of analysis; preventive maintenance reports and record, qualification and validation protocols and reports.

All documents scrutinized were well written, detailed, updated as per master SOP and were traceable hence provide evidence of conformity to GMP requirements.

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, **Eugia Pharma Specialties Ltd, Plot No. 5-38, Survey No. 550, 551 & 552 Kolthur Village, Shameerpet Mandal, Medchal Malkajgir, District - Medchal , Pin 500101 Telangana State, India** was considered to be operating **at an acceptable level** of compliance with EAC GMP Compendium for the **manufacturing Oncology OSD (tablets , hard gelatin capsule and soft gelatin capsule) and Hormones (Injectable and tablets)**.

This report shall be valid for 3 years from the date of approval unless forms and operations herewith are changed or the site is no longer considered to be in compliance with current GMP requirements.

Part 4: References

1. Tanzania Food, Drugs and Cosmetics Act, Cap 219.
2. EAC- *Good* manufacturing *Practice Compendium, (2014), Technical Documents for Harmonization of Medicines Regulation in the East African Community.*
3. TFDA *Good Manufacturing practices manual and SOPs,* Tanzania Food and Drugs Authority, Dar-es-Salaam, Tanzania.
4. Eugia Pharma Specialities Ltd – Site Master File.