TMDA/DMC/MCIE/F/001

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

BIOLOGICAL E. LTD, TELANGANA, INDIA
PUBLIC GMP INSPECTION REPORT

11th December 2020.

Part 1: General information about the company

Manufacturers details	
Name of manufacturer	Biological E. Ltd
Corporate address of manufacturer	Biological E. Ltd, Plot No. 1, Biotech Park, Phase -II, Kolthur (V), Shameerpet, Medchal-Malkajgiri District, 500 078, Telangana, India.
Inspected site	
Name & address of inspected manufacturing site	Biological E. Ltd, Plot No. 1, Biotech Park, Phase -II, Kolthur (V), Shameerpet, Medchal-Malkajgiri District, 500 078, Telangana, India.
Unit/ block/ workshop number	Not Applicable
Inspection details	
Date of inspection	15th – 16th April 2019
Type of inspection	Renewal GMP Inspection
Introduction	
General information about the company and site	Biological E. Limited is located at Shameerpet, Medhcal-Malkajgiri District, Telangana, India. The facility has been issued a license by the local FDA to manufacture bulk vaccines, blending, filling and packaging of final lots including Tetanus Toxoid (TT), Diphtheria Tetanus and Pertussis (DTP). Products registered in Tanzania included adsorbed Tetanus Vaccine single dose and DTwP – rHepB – Hib Vaccine Liquid Single Dose.
History	The facility was inspected and approved by the local regulatory Authority and issued with GMP certificate The facility has also been inspected and approved by other NMRA.

	This was renewal GMP inspection following expiry of the previous GMP inspection conducted on 2nd June 2014.
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	The inspection focused on production lines for products registered in Tanzania
Out of scope	Production lines for which application for product registration had not been submitted
Production lines inspected by TMDA	Vaccines manufacturing s line
Abbreviations	**Meaning**
AHU	Air Handling Unit
EAC	East African Community
GMP	Good Manufacturing Practices
HVAC	Heat Ventilation and Air Conditioning
RLAF	Reverse Laminar Air Flow
SOP	Standard Operating Procedures
TMDA	Tanzania Medicines and Medical Devices Authority

Part 2: Brief summary of the findings and comments

1. Personnel

The facility had adequate number of personnel with appropriate qualifications and experience in production and quality control of biological products. Organization chart and job descriptions for the key personnel indicated that heads of Quality Control and production were independent. GMP Training was provided to personnel as per respective standard operating procedure (SOP), records were reviewed and found adequate.

All personnel, prior to and during employment were medically examined while personnel engaged in production, maintenance, and animal care were appropriately vaccinated. Medical examination and vaccination records were in place.

2. Premises

i. Layout and Design

The base flooring and external super structure of all blocks were built with reinforced cement concrete (RCC). The external walls were made up of plastered bricks and painted to give smooth crack free impervious surface.

In production and quality control laboratory, all internal walls were partitioned with pre-fabricated pre-engineered sand-witched modular panels with injected polyurethane foam (PUF) as insulating material. The floor was made of monolithic PVC to provide smooth finish and all corners were concealed with coving and joints of modular panels covered with silicon sealant to facilitate cleaning. All doors were constructed with powder coated galvanized iron with a polyurethane coating and had a double glazed viewing panels.

In experimental animal house blocks, the interior partitions were made up of bricks and painted with enamel and the flooring was of ceramic tiles.

The layout was designed to provide for a unidirectional flow of materials and personnel with separate entries for the same.

ii. Sanitation and Hygiene

The facility was provided with dedicated areas for sampling of active and inactive pharmaceutical ingredients. Production areas had separate airlocks for personnel and materials with interlocking doors, separate change rooms and air shower for personnel working in core production areas.

Primary, secondary and tertiary gowning procedures in changing rooms were provided to facilitate proper gowning and therefore prevent contamination. All workers were found in clean uniforms.

3. Production

Access to production area was restricted to authorized personnel. The facility had separate areas for storage of raw materials, packaging materials and finished products.

Production building consisted of blending and filling block, bacteria vaccine block which also had bioprocess suite I&II, purification suite, conjugation suite I&III, meat block, -20^0 C deep freezer and $2\text{-}8^0$ C freezer. The recombinant vaccine block consisted of bio process, purification areas, and packaging hall which had packaging areas and finished goods store. There were proper separations between the packaging lines to avoid mix-ups.

4. Quality Control

The Quality Control laboratory was composed of wet chemistry, instrumentation and microbiology section. Apart from these, other sections available included stability chambers and controlled sample rooms. Procedures were in place for sampling and testing of starting materials, packaging materials, intermediates, water, critical animal bulk and finished products, environmental monitoring and stability testing.

Some of analytical testing activities were outsourced from approved technical assistant centers or laboratories. In vivo testing service was outsourced from approved centers when required. Adequate number of personnel with appropriate qualification were available to carry out analytical tests.

Stability chambers were set to cover storage conditions at 25^0C /60%RH, 30^0C /65%RH, 30±2^0C/75±5%and 2^0C - 8^0C. Products under stability studies were observed to be stored in the chambers and appropriate log books were available.

5. Equipment

The facility had 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. Water Treatment System

Municipal or bore well water was pre-treated by passing through series of filters before passing through reverse osmosis system. Pre-treated water then passed through several filtration systems (multi grade filters, ultrafiltration, cartridge and bag filtration) and chemical treatment to obtain purified water. Purified water was continuously in circulation through a distribution loop to inhibit microbial growth.

Purified water was sampled at identified sampling points and tested for chemical attributes and microbiological parameters as per standard operating procedures (SOPs) and specifications. Schematic drawings as well as SOP for water treatment and daily records were available at the site. Cleaning and sanitization of purified water and distribution system was performed on scheduled frequency as per procedure. Log book for cleanliness of water treatment plant was found in place.

7. Heating, Ventilation and Air Conditioning

All Personnel Air Locks and Materials Air Locks had door interlocking systems and the subsequent doors were opened through a time delay system to ensure that differential pressures are properly maintained.

There was a dedicated AHU to feed fresh air to all AHUs. Exhaust and Relief air connections were connected to the HEPA filters to release air to the atmosphere. Reverse laminar airflow (RLAF) was provided in sampling and dispensing rooms. The HVAC system was qualified as per protocols and records were available.

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, including the observations listed in the report**, Biological E. Ltd, Plot No. 1, Biotech Park, Phase-II, Kolthur (V), Shameerpet, Medchal-Malkajgiri District,500 078 , Telangana, India**, (Vaccine production line) 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. EAC- *Good* Manufacturing *Practice Compendium, (2014), Technical Documents for Harmonization of Medicines Regulation in the East African Community*
2. GMP Inspection Manual Doc. No. TFDA/DMC/ MI&E/M/001.
3. Biological E. Ltd GMP Inspection report April, 2019.
4. Tanzania Food and Drugs and Cosmetics Act, Cap 219.