THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

ADVANCE AGROCHEMICAL AND VETERINARY PRODUCTS INDUSTRIAL CO., (CHEMVET), AMMAN - JORDAN

PUBLIC GMP INSPECTION REPORT

March, 2025

General information about the company

Manufacturers details	
Name of manufacturer	Advance Agrochemical and Veterinary Products Industrial Co. (CHEMVET)
Corporate address of manufacturer	King Abdullah II, Industrial City, Al Azraq St 250, Amman, P.O. Box 294 code 11512, R2V6+M4 Amman Jordan Tel: 0096264022640 Website: www.chemvetjo.com
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Same as above
Unit/ block/ workshop number	General Block for manufacturing general veterinary pharmaceutical products - Oral liquid, Oral powder, oral gel, tablets, ointment and aerosol spray
Inspection details	
Date of inspection	9th &12th May, 2024
Type of inspection	GMP Pre-registration Inspection
Introduction	
General information about the company and site	Chemvet was located at King Abdalla II Industrial City, Al Azraq St 250, Amman R2V6+M4 (the population free zone), Amman, Jordan. The facility had manufacturing license issued by Ministry of agriculture /veterinary department for (oral liquid, oral powder, oral gel/paste, oral tablet/bolus, ointment/ cream, aerosol and feed additives production.
History	The facility was inspected by Jordanian Ministry of Agriculture/Veterinary & Animal Health Department and Regulatory Authority of Egypt and complied with the requirements of

	GMP for production of general Oral liquid, Oral powder, Oral tablet/ bolus, Oral gel/paste, Ointment/ cream and Aerosol spray
Brief report of the activities undertaken	
Areas inspected	Areas inspected included external surroundings, utilities, warehouses, manufacturing areas and quality control laboratory. Other GMP quality elements that were also covered, include; i. qualification and validation ii. handling complaints and recalls iii. vendor evaluation and contract agreements iv. premise layout v. sanitation and hygiene vi. personnel vii. equipment viii. documentation
Restrictions	GMP inspection was restricted to production line which manufacture products registered or applied for registration in Tanzania
Out of scope	Production lines whose products are neither applied for registration nor registered in the country
Production lines inspected by TMDA	General pharmaceuticals for veterinary use inform of Oral liquid, Oral powder, oral gel, tablets, ointment and aerosol spray
Abbreviations	**Meaning**
AHUs	Air Handling Units
API	Active Pharmaceutical Ingredient
AVUs	Air Ventilation Units
BMR	Batch Manufacturing Record
BMS	Building Management Systems
BOD	Biochemical Oxygen Demand
BPR	Batch Packaging Record
CAPA	Corrective action and Preventive Action
CIP	Cleaning In Place
EDI	Electrode ionization

EMS	Environmental Monitoring Systems
ERP	Enterprise Resource Planning
FDA	Food and Drug Authority
FPP	Finished Pharmaceutical Products
FTIR	Fourier Transform Infrared Spectroscopy
GC	Gas Chromatography
GMP	Good Manufacturing Practice
HEPA	high-efficiency particulate air
HPLC	High Performance Liquid Chromatography
HVAC	Heating, Ventilation and Air Conditioning
LAF	Laminar Air Flow
NMRA	National Medicine Regulatory Authority
OOS	Out of Specification
OOT	Out of Trend
OSD	Oral Solid Dosage form
PLC	Programmable Logic Controller
PQR	Product Quality Review
QA	Quality Assurance
QC	Quality Control
QRB	Quality review Board
SCADA	Supervisory Control and Data Acquisition
SOP	Standard Operating Procedure
TOC	Total Organic Carbon
WHO TRS	World Health Organization Technical Series Report
WTP	Water Treatment Plant

Part 2: Brief summary of the findings and comments

1. Personnel

The manufacturer had sufficient number of technical staff with necessary qualifications and experience to carry out the tasks assigned. Personnel met were knowledgeable about principles of GMP which proved that they received basic and on job training on principles of GMP relevant to their needs and in accordance with GMP training schedule in place.

The organizational chart was reviewed whereby key responsibilities were held by permanent staff, head of production unit and quality unit were independent of each other.

There was a procedure in place for medical checkup. Pre-employment health check was done for new employee while all other personnel were checked periodically. Adequate measures were taken for personnel hygiene and personnel were observed properly dressed with neat and clean gowns, gloves and masks.

2. Premises

a. Layout and Design

Facility had two buildings of which the first building housed warehouses, utilities (WTP, compressed air, AHU and boiler) and administration while second building housed QC lab and R&D laboratory. The walls were made of cement and galvanized steel with smooth electrostatic metal coated and epoxy finishing with non-shrinkable hard epoxy resin to prevent accumulation of dust and facilitate cleaning. The floor was made of epoxy and self-level with smooth surface finishing of non-shrinkable hard epoxy resin and the ceilings were made of RCC and walkable panels with surface finishing of electrostatic metal coated false sealing. Lights were flushed with ceiling. Air supply diffusers were placed on the ceiling and return risers were placed at the bottom of the walls.

All areas were provided with adequate working space for orderly and logical placement of equipment and materials to avoid mix-ups and cross-contamination. was designed for unidirectional flow of materials and personnel, the facility

b. Sanitation and Hygiene

Personal hygiene at the facility was considered appropriate with respect to the manufacturing and packaging operations carried out, and in line with the GMP guidelines. There were procedures and pictorial illustrations in place for gowning on entry and exit to and from manufacturing area and medical health check procedure in place for occupational health of all employees and casual workers.

Validation of cleaning procedure was conducted to assure that the procedure for cleaning equipment was consistent and in-line with the defined acceptance levels. Cleanliness of production areas was adequately done at defined frequency using appropriate cleaning agents. Records were maintained.

3. Production

Generally, production operations followed defined procedure and production plan in place, BMR and BPR were maintained and properly filled. Weighing and measuring devices were of suitable accuracy for the intended use and records were maintained in

respective logbooks. Temperature, relative humidity and differential pressures were monitored in the production area and the same were observed to be within limits and records were availed. Environmental monitoring was performed during filling using settle plates and particulate counters and the records were verified during document review. Punches and dies were stored in separate room, usage and cleaning records were maintained.

a. Oral Liquid production line

Raw materials required for preparation were weighed then transferred to the mixers via containers and transferring carts. Then the materials were added and mixed according to the approved manufacturing steps.

After completing the mixing process, a sample of the semi-finished product was taken to the laboratory department to conduct the required tests based on the approved specification for the product and released according to the laboratory test result. Prior to filling process, the bottles were cleaned by blowing with compressed air, then filling the product and weight verification by random sampling of filled bottles during the entire filling stage, then bottle capping and sealing. Sealed bottles passed through the packaging line were printed labels with batch number were affixed, if required on the packages or caps, then the label was stack, then shrink if required, and then the packages were placed in boxes or cartons.

Random samples of FPP were taken to the laboratory department to conduct the required tests based on the approved specification for the product. Hence, the product was released according to laboratory test result and transferred to the finished goods warehouse.

b. Dry powder production line

Facility had blender machine in the powder mixing room with capacity of 250L and filling machine with capacity of filling 800l/hr. After blending of dispensed material, the powder is then packed in jars and sachets. Moisture content was monitored in the powder production line.

c. Tablet production line

The manufacturing process involved dispensing of raw materials, verification of dispensed raw materials, mixing of API with excipient, granule regulation, sieving, final blend, tableting, coating, blister packaging, packing, plastic sealing and boxing. In process control test including moisture content, appearance and color, hardness, thickness, friability, disintegration were checked at start up and end of batch.

d. Aerosol production line

The manufacturing process involved dispensing of raw materials, mixing via containers and transferring carts. Then the materials were added and mixed according to the approved manufacturing steps.

After completing the mixing process, a sample of the semi-finished product was tested based on the approved specification for the product. Usually, the appearance, color, density and pH were tested in addition to the assay of the active ingredient.

Then the mixture was released based on laboratory test results followed by filling process and weight verification by random sampling of filled bottles during the entire filling stage. Valves were then placed on the filled cans with compressed gas; fill volumes / weights verification and leak test of sealed cans were checked by random sampling. Actuators and product information were then affixed to the aerosol cans before packing in boxes and cartons.

Random samples of final product were analyzed based on the approved specification for the product and released according to laboratory test result then transferred to the finished goods warehouse.

4. Quality Control

The facility had a quality control (QC) laboratory which was separated from production areas. The QC laboratory was located in the administrative block and divided into different sections such as sample receiving area which was access-controlled, chemical laboratory, instrumentation rooms, microbiology section, stability room, and retained sample room. The QC laboratory was responsible for analysis and release of dosage forms, active ingredients, raw materials, intermediates, packing materials and environmental monitoring. The procedures and logbooks, calibrations, daily weight checks temperature and humidity monitoring records were in place.

Raw, packaging materials and finished goods were tested as per specifications using validated analytical methods. All incoming materials were sampled according to predefined sampling plan and given unique analytical reference number.

Retention samples were kept in a secured and temperature-controlled room, retention sample register and samples of each batch finished product produced were kept with double quantity of full testing. Annual check for the sample was performed according to the company procedures. The facility had three stability studies chambers set at the

following condition 40^{0}C/75% RH for Accelerated conditions and two stability chambers for long term stability studies set at 30^{0}C/75%RH and 30^{0}C/65%RH.

The facility used primary and working standards with specified shelf life which were stored in a temperature-controlled refrigerator. The working standards were prepared from approved lot of the raw materials and qualified against the pharmacopeial chemical reference standard. The register for the use of reference standard was maintained. The list of primary standards was maintained and their validity in the respective on web-catalogues confirmed.

The facility had procedure in place for validation and verification of analytical test to ensure that they meet the requirements for the intended analytical applications. Reagent and solutions were handled as per procedure with detailed information regarding to preparation and standardization of volumetric solutions, glassware used for measuring in the facility were of class A. Reagents and solutions were labeled with solution/reagent name and information on shelf life, list of QC reagents and solutions was well maintained.

5. Equipment

The equipment in all manufacturing lines was well designed and located to suit the operations and permit for effective cleaning. Manufacturing equipment were qualified, requalification, revalidated and equipment maintenance schedules were in place and adhered to so as to ensure that all equipment function properly and meet their intended purposes. All equipment were affixed with both calibrations, maintance and machine status label

6. Purified water System

The source of water was a municipal water. Water was pumped and passed through a chlorine dosing followed by a sand grade filter, carbon filter, double softeners to produce soft water that was stored in HDPE storage tank. From soft water tank, water was filtered through 5µm filter before treatment with Sodium Metabisulphite. After removal of chlorine by Sodium Metabisulphite water was passed through double RO system, electrical deionizer, UV lamp and then 2µm filter. Water was then stored in the PW tank which was collected in SS316L and water was circulated at ambient condition below 15-25^{0}C to prevent microbial growth.

7. Heating, Ventilation and Air Conditioning

The heating, ventilation and air conditioning (HVAC) system consisted of eight (8) Air Handling Units (AHUs) with the aim of supplying filtered air to dedicated areas such as

warehouse, production and quality control for the purpose of preventing mix-ups and cross contamination. Smoke detector was installed in the main duct to detect smoke in case of fire and stops AHU.

The AHU was consisted of blower, chilled water coil, hot water coil, dehumidifier and filters. As per schematic diagram displayed on HVAC system and physical inspection conducted, it was observed that the fresh air entered the AHUs through the primary filter of 5µm pore size followed by dehumidification and cooling then to the secondary filter of 1µm pore size to the HEPA filter where clean air was supplied to the production areas.

AHU supplied 10% fresh air to maintain differential pressure between 5 – 15 Pascal between adjacent areas and number of air changes were NLT 20 air change/hour.

8. Document Review

The company had two types of documentation systems (Electronic system and paper-based system). The documents related to assurance of quality and safety of pharmaceutical products being manufactured, were prepared by the quality management department and strictly closely followed and controlled. Documentation was designed, prepared, reviewed and distributed to users according to procedures in place. Procedure for preparation, issuance, recording, retrieval, storage and destruction of documents and records were in place. Documents were retained for a period of 5 years and electronic data was backed up daily and stored in flash disk for a period of six (6) months.

Part 3: Conclusion

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection **Advance Agrochemical and Veterinary Products Industrial Co. (CHEMVET) located at King Abdalla II Industrial City, Al Azraq St 250, Amman R2V6+M4 Amman Jordan** is considered to be operating at an acceptable level of compliance with with TMDA Good Manufacturing Guidelines for Veterinary Medical Products, Second edition, April, 2022 for the production of General Veterinary products in form of oral liquid, oral powder, tablets, ointment and aerosol spray.

This TPIR will remain valid until 15th June, 2027, provided that the facility will remain compliant following any inspections conducted in the period.

Part 4: References

1. Tanzania Medicines and Medical Devices Act, Cap 219

2. TMDA (2018) Good Manufacturing Practices Enforcement Regulations, GN 295
3. TMDA SOP for conducting the inspection of pharmaceutical manufacturing facilities; TMDA/DMC/MCIE/SOP/008, effective date April 2022,
4. Advance Agrochemical and Veterinary Products Industrial Co. (CHEMVET) site master file SMF/QA Revision 5 dated 24/01/2024
5. TMDA (2022) Good Manufacturing Guidelines for Veterinary Medical Products, Second edition.