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REV.#. 01



THE UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH



TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

HEBEI KEXING PHARMACEUTICAL CO. LIMITED, CHINA
PUBLIC GMP INSPECTION REPORT

March, 2025



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General information about the company

Manufacturers details	
Name of manufacturer	Hebei Kexing Pharmaceutical Co., Limited
Corporate address of manufacturer	No. 114 Changsheng street, Luquan Development Zone, Shijiazhuang City, Hebei, China. Tel: +86-311-80677112/ +86-311-806771113 E-mail: kexing@kexingpharma.com
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Same as above
Unit/ block/ workshop number	
Inspection details	
Date of inspection	14 th - 15 th October, 2024
Type of inspection	GMP Renewal Inspection
Introduction	
General information about the company and site	This manufacturing site was located at the Luquan development zone at Shijiazhuang City in Hebei Province. The company had operation license No. (2022) SYZ 03011 issued on 31 st May, 2022
History	The facility had certificate of Good Manufacturing Practices for Animal Drugs number (2022) Veterinary Drug No. 03018 valid from 31/05/2022 to 30/05/2027 issued by the Department of Agriculture and Rural Affairs of Hebei Province, China The facility was inspected by Nigeria Food and



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	Drug Authority (NAFDAC) on 06 th November, 2023 and issued cGMP Certification
Brief report of the activities undertaken	
Areas inspected	Area inspected followed the flow of production starting from the raw materials and packaging materials warehouse, production areas, packaging areas, quality control laboratory (chemistry and microbiology), stability room, and retention samples storage rooms, and utilities including the water treatment plant (WTP) for purified water and air handling unit (AHUs).
Restrictions	N/A
Out of scope	Production lines whose products are neither applied for registration nor registered in the country
Production lines inspected by TMDA	This inspection covered six manufacturing lines for general veterinary products that included, i) Sterile solution for injection (SVP and LVP) ii) Oral dosage form (oral tablets, powder and liquids) iii) Disinfectants, pesticides and premix. iv) Herbal products
Abbreviations	Meaning
AHU	Air Handling Unity
FPP	Finished Pharmaceutical Products
GMP	Good Manufacturing Practices
RO	Raw Water
OSD	Oral solid Dosage
QA	Quality Assurance
QC	Quality Control
SVP	Small volume Parenteral
LVP	Large Volume Parenteral
WTP	Water Treatment Plant
TOC	Total organic Carbon



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Part 2: Brief summary of the findings and comments

1. Personnel

The company had dedicated an adequate number of staff to carry out daily activities in all areas i.e., warehouses, production, quality control, quality assurance, and other supporting activities so as to ensure the smooth running of the activities at the site. It was found that production and quality control key technical personnel were totally independent from each other in job execution and decision-making. The production manager reported to plant manager while quality control reported to vice president. The appointment letters and job responsibilities of the key personnel were reviewed. In general, the job descriptions, responsibilities, and duties of the key personnel appeared to be adequately written and implemented

the facility had SOP for conducting training to new employee and on-job training to staff. A sample check of records revealed that the personnel in production department were trained on cGMP and refresher training was conducted annually as per SOP requirements. An annual review of a personnel training record was carried out and it was observed that all training conducted for the year 2024 was completed recorded and supported with the training attendance list.

Medical examination was conducted by designated hospital. The contract agreements between Hebei Kexing Pharmaceutical Co., Limited and the hospital were reviewed and it was noted to be valid for one year. The medical examination records for selected employees were reviewed and found to be conducted by an approved clinician from the approved hospital as per SOP requirements, once every year.

2. Premises

a. Layout and Design

The premise constituted three buildings, building number 1 had four of which the first floor was the workshop of manufacturing large volume intravenous injection. The second floor was the workshop of manufacturing of small volume injection. The third and fourth floors were for manufacturing of non-sterile liquid formulations.

Production building number two (2) had three floors. Third floor was involved in the manufacturing of tablets and granules. Other floors were used for storage and production of herbal products which were not part of this inspection.



The third building was still under construction and therefore was in the scope of inspection at this time around.

Facility layout and buildings were designed to allow for unidirectional flow of material, from the raw material store to the finished goods store. All buildings were constructed using reinforced cement concrete frame structures, walls had smooth finishing to allow for easy cleaning. Floors and walls were designed with a smooth finish with no crevices or rough surfaces, wall to floor, wall to ceiling and wall to wall joints were covered to facilitate cleaning. White polyurethane paint was used to paint all the internal walls of critical production areas. All windows were flushed with the wall surface on both sides of the wall.

b. Sanitation and Hygiene

During the inspection, the cleanliness of all critical areas (i.e., production areas, quality control laboratory, raw materials and finished product warehouses, washing area, cleaned equipment storage area, and utility buildings) was noted. Premises and equipment were generally cleaned according to established validated procedures.

The facility had changing rooms and washrooms equipped with washing basins and sanitization points. Change rooms were well-ventilated, maintained, and had documented procedures with pictorial presentations for gowning, de-gowning, hand washing, and dress code. The change rooms were also provided with changeover cross bench, storage lockers, hand washing, and disinfection facilities.

3. Production

A. Sterile Small and Large Volume Injection – Blow fill and seal (BFS)

Oral soluble powder preparation was manufactured in second floor of the second (2) building. The small volume parenteral was carried out in second floor of the building number one. Manufacturing of Sterile solution for infusion involved the following stages; material dispensing, solution preparation and filtration in class C area, bottle injection, mold, stretch and blow in class C area, filling in Class A clean area with background of class C, terminal sterilization, visual inspection and packaging.

Approved bulk solution was then transferred to filling vessel through pre-filter 0.45 μ and then 0.22 μ then filling. Filter integrity test was performed before and after filtration and recorded in the batch manufacturing record.

Manufacturing processes were initiated as per the BMR and the sequence of activities was properly followed and recorded in the BMR. Line clearance was performed as per respective procedures, checklists were properly filled. This was evidenced from the



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executed batch manufacturing record for Sodium Chloride 0.9%. The BMR were signed, dated, and properly filled. Checks on yields and reconciliation of quantities were carried out and variations in the percentage yield of the product were observed.

In-process controls were performed for the solution before filling for pH and assay and after filling tests for checking for leakage, particles, seal rejects and fill weight were performed. Visual Inspection was performed as per the procedure and included a check for presence of particles and sealing defects.

During manufacturing, environmental monitoring was done for viable and non - viable particulates. Settle plates and particulate counters were observed during filling. Personnel monitoring was conducted after every shift. Terminal sterilization was done at 115°C for 30 minutes by a super-heated steam sterilizer. Biological indicators i.e., *Bacillus subtilis* was used to determine the effectiveness of the sterilization process for every batch sent for sterilization.

B. Sterile Small and large Volume for Injection-Glass bottle and vials

Large volume parenteral were manufactured in first floor and third floor of the first building and the small volume parenteral was carried out in second floor of the building number one.

The manufacturing process of large and small volume injectables in vials and bottles involved materials weighing, then preparation of concentrated solution in concentrate preparation tank. The concentrated solution was filtered and then transferred to dilute solution preparation tank where dilution using water for injection was carried out. After mixing in dilute solution, mixing tank, the solution was filtered using series of 1 µm and 0.2 µm filter size and then transferred via pipe to filling area. Vial and bottles washing was done by using purified water and water for injection and then dried by using compressed air before they were subjected to depyrogenation tunnel. Stoppers were washed with WFI and then sterilized. Aluminum-plastic composite caps were also washed with WFI and dried before capping. Filling, sealing and capping were done in class A area. After filling the vials were terminally sterilized by using qualified autoclave.

Manufacturing processes were initiated as per the BMR and the sequence of activities was properly followed and recorded in the BMR. Line clearance was performed as per respective procedures, checklists were properly filled. Checks on yields and reconciliation of quantities were carried out and variations in the percentage yield of the product were observed.



C. Bolus and Granules

Bolus and granules were manufactured in third floor of the second building. The manifesting process involved dispensed materials that were transferred to staging area via material elevator. Then the dispensed materials transferred to feeding room equipped with vacuum feeding machine used to transfer the materials to granulation machine for granulation process. Then the wet granules were dried and lubricated using Magnesium stearate. The Lubricated blend was tested for water content and content uniformity. Then the lubricated blend was transferred to compression room equipped with compression machine for bolus and tablets production. In process testing conducted were friability, weight variation, hardness and disintegration so as to ensure product was meeting pre-determined specification. The approved bolus was sent to primary package hall provided with blister packaging machine. The Bolus packed in blisters was transferred through conveyer to secondary packaging room where blisters were packed in secondary carton and boxes.

Moreover, for granules for oral, the granules were transferred to filling machines in sachets and transferred through conveyer to secondary packaging room where blisters were packed in secondary carton and boxes.

D. Oral Solution

Oral solution preparation was manufactured in fourth floor of the first building. The manufacturing process of oral solution included dispensing of materials that were transferred to staging area via material elevator. Then materials were transferred to dispensing and weighing room then materials transferred to feeding room equipped with vacuum feeding machine used to transfer the materials to mixing tank. After the bulk complied with release test, the solution is transferred to the bottle filling machine through dedicated pipes where the filling, capping and sealing were carried out. Then the filled bottle was transferred to Secondary packaging and transferred to the storage area by coded robot.

E. Oral Soluble powder

Oral soluble powder preparation was manufactured in second floor of the second (2) building. The manufacturing process of oral soluble powder involved dispensing of materials that were transferred to staging area via material elevator. Then materials were transferred to dispensing and weighing room then to feeding room equipped with vacuum feeding machine used to transfer the materials to double column mixer with identification number YHJ-05 with capacity of 2,000 L. After mixing was then transferred into powder premix packing machine, where primary packing was carried out in sachets and after that was transferred to secondary packaging area.



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4. Quality Control

The facility had a quality control laboratory which was divided into three (3) sections i.e. Microbiology laboratory, Chemical Laboratory and instrumentation laboratory. The laboratories were spacious, well organized, and equipped with various equipment

The quality control department was responsible for developing specifications and testing procedures. The approved specifications and test procedures in the prescribed format were available for all manufactured products including those that have been applied for marketing authorization in Tanzania. Both in-house and pharmacopoeia methods were used for analysis for the raw materials and finished products. The facility had a dedicated room for the storage of control samples for both raw materials and finished products. The retention sample rooms were fixed with temperature and humidity monitoring devices and the conditions were maintained below 25°C and 65% RH and were retained at least one year after expiry

The microbiology laboratory performed microbial limit tests, environmental monitoring, and water tests. The cultures were handled in the biosafety cabinets (level 1) with a background of grade C. Microbial limit test was performed under LAF bench with a background of grade C.

5. Equipment

Adequate GMP equipment was available. They were of appropriate design (cGMP type), adequate in size and properly installed to suit their intended operations, facilitate effective cleaning and maintenance. Part of equipment that was in contact with drug products were made from SS316L material. The same were cleaned, qualified as per procedures and were functioning properly. Status labels were affixed on equipment.

Preventive Maintenance of production equipment was carried out as per preventive maintenance program and respective procedures. Equipment was calibrated as per calibration plan.

6. Purified water System



The facility had a well-designed water treatment plant used for the generation of purified water. The potable water was sourced from the city. The potable water was purified by dosing the chlorine and alum followed by filtration through multi grade filters and activated carbon and then pass through UV light.

Then water was passed through a UV purifier and filtered through 5 μ cartridge filter. The purified water was stored in a 1000 Litres SS tank and distributed through pipes to various user points. The SOP for sampling and testing of purified water, for monthly trending of water and for Sampling and Testing of Water were reviewed and accepted.

Sampling points were well identified in the entire system as per qualification reports and were traceable in the environment monitoring logbook. Testing parameters such as pH, conductivity, particulate, microbial contaminations, and TOC were conducted for water quality analysis

The system was cleaned and sanitized by using pure steam maintained at 121°C every 3 months as per Operating & sanitization of PW distribution system and operating & sanitization of WFI distribution system

The WFI is collected in the SS tank 10,000 L. WFI was circulated to user points through the SS316 secondary loop and maintained at NLT 80°C. Purified and WFI and their supplying loops were kept in continuous circulation.

7. Heating, Ventilation and Air Conditioning

The facility had air handling units designed with G4, 10 μ m and F8, 3 μ m filters and the HEPA filter of 0.2 μ m at the room. Air supplied to all critical areas was filtered through HEPA filters H14 of 0.2 μ m pore size with 99.995% efficiency. In other non-critical areas, air was filtered through 3.0 μ m filters (raw material, quality control & packing areas) and 5 μ m filters (finished product warehouse). The microbiological testing room was provided with a separate AHU with terminal HEPA filters of 0.3 μ m pore size with 99.97% efficiency.

8. Document Review

In review of these documents, it was generally observed that the documents were appropriately prepared, reviewed, and approved as per the procedure and format given in the standard operating preparation for the preparation of SOPs



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Part 3: Conclusion

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, **Hebei Kexing Pharmaceutical Co., Limited, Shijiazhuang City, Hebei, China** was considered to be operating at an acceptable level of compliance with **TMDA Good Manufacturing Practice Guidelines for Veterinary Pharmaceutical Products, Second Edition, April, 2022** for Manufacturing and packaging of General Veterinary products sterile (SVP and LVP) and Oral dosage in for of (oral bolus, tablets, granules, powder and liquids) of veterinary medicinal products.

This TRIP 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. Hebei Kexing Pharmaceutical Co, Limited, Shijiazhuang City, Hebei, China, 2024 GMP inspection report.
2. TMDA, (2003)., Tanzania Medicines and Medical Devices Act, Cap 219, Tanzania Medicines and Medical Devices Authority, Government Printers, Dar es Salaam, Tanzania
3. TMDA Good Manufacturing Practice Guidelines for Veterinary Pharmaceutical Products, second edition, April 2022
4. TMDA, (2018)., Tanzania Medicines and Medical Devices (Good Manufacturing Practices Enforcement) Regulations GN No. 295. Tanzania Medicines and Medical Devices Authority. Government Printer, Dar es Salaam, Tanzania
5. TMDA Good Manufacturing Practices Manual and SOPs, Tanzania Medicines and Medical Devices Authority Dar-es-Salaam, Tanzania.
6. TMDA, RIMS 2.0.