THE UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

AMMAN PHARMACEUTICAL INDUSTRIES CO.,
KING ABDULLAH II, INDUSTRIAL CITY, AMMAN 1152, JORDAN

PUBLIC GMP INSPECTION REPORT

Date: 5th March, 2025

General information about the company

Manufacturers details	
Name of manufacturer	Amman Pharmaceutical Industries Co. Limited
Corporate address of manufacturer	King Abdullah II Ind. City, State, Sahab, Amman, Jordan, P.O. BOX 89, Postal Code: 11512
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Amman Pharmaceutical Industries Co. Limited Primary Facility -Building 108, Street 3, King Abdullah II, Industrial City, Amman, 1152, Jordan Associated Facility- Warehouse: Building 112, Street A3, King Abdullah II, Industrial City, Amman 1152, Jordan.
Unit/ block/ workshop number	1
Inspection details	
Date of inspection	07th - 08th May, 2024
Type of inspection	GMP Re- inspection
Introduction	
General information about the company and site	Amman Pharmaceutical Industries Co. Limited operated under a manufacturing license (No. 2/16/ML-General/7/2021) issued by the Jordan Food and Drug Administration, valid until November 2024. The facility manufactured a range of sterile products (including eye drops, ear, nose drops, ointments, and gels) and non-sterile products (such as solutions, lotions, suspensions, and syrups). It also handled primary and secondary packaging and batch release with or without quality control testing.

	The facility held a valid GMP certificate from the Jordan Food and Drug Administration and has obtained 19 GMP certificates from various National Regulatory Authorities (NRAs) across countries such as Kenya, Uganda, Egypt, Saudi Arabia etc.
History	Amman Pharmaceutical Industries (API) was established in 1989 as one of the first pharmaceutical companies in the MENA region, pioneering the production of niche branded generics in ophthalmology, nasal, oral and dermatology. Over the years, API has grown into a leading pharmaceutical manufacturer in the MENA region, expanding to 8 production lines and producing 152 registered products. The company exports its products to more than 25 global markets and employs over 242 people. API's success is built on its focus on differentiation, making it a prominent player in the region's pharmaceutical industry.
Brief report of the activities undertaken	
Areas inspected	The inspection covered warehouses for incoming raw materials and finished goods, along with production areas for manufacturing and packaging. Quality Control (QC) laboratory and essential utilities, such as a water treatment plant, HVAC system, compressed air, effluent treatment plant and pure steam generation system.
Restrictions	N/A
Out of scope	N/A
Production lines inspected by TMDA	The inspection was based on the manufacturing of sterile eye, ear, nose drops, sterile eye ointment, topical semi- solids, oral liquids, non-sterile ear and nasal drops and metered-dose nasal spray, non-sterile sprays

	Aerosols (BOV).
Abbreviations	**Meaning**
N/A	Not applicable

Part 2: Brief summary of the findings and comments

1. Personnel

The facility employed a total of 262 personnel who were qualified, competent, and experienced in their respective roles. Personnel were organized across various departments including production, quality section, warehouse, engineering and others, with their positions clearly defined in the organizational chart. The organization chart demonstrated the independence of key personnel in performing their duties, particularly within the Production and Quality Control departments, where personnel positions were independent of each other. The Quality Control and Quality Assurance Managers reported to the Head of Quality, and appointment letters along with job descriptions for all key personnel were reviewed, confirming the defined responsibilities for each position.

Training for personnel was conducted according to approved procedure. Various categories of training were provided, including on-the-job training, pre-job training for new employees, those transferring roles, and employees returning to work. Technical retraining was arranged by each department based on the introduction of new products, methods, processes, and equipment. An annual training plan for staff, covering the period from January 2023 to December 2024, was reviewed and verified, ensuring that all staff members received relevant and timely training.

Medical examinations were performed as per approved procedure for personnel health. The procedure outlined the requirements for both pre-employment and post-employment medical exams, including checks for communicable diseases and basic eye tests. All employees were required to undergo a medical examination annually and at the time of recruitment. A valid contract agreement with a private doctor for the service provider was in place, and medical examination records for selected employees were readily available for review.

2. Premises

a. Layout and Design

The facility's building construction was designed to prevent the entry of rodents, birds, or insects, with traps strategically placed at all entry points to the production and warehouse areas. It included change rooms to ensure personnel hygiene and was constructed to promote the unidirectional flow of materials, personnel, and effective

cleaning and maintenance. The walls and floors featured smooth surfaces with covings between walls, floors, and ceilings.

The storage of finished goods was housed in a separate building from production, with facilities for the efficient transfer of materials from the warehouse to production and finished goods from production to the warehouse. Airlocks were provided for the entry of equipment, materials, and personnel into clean areas, ensuring the control of sterile production areas.

The Quality Control laboratory was located separately from production and warehouse areas. It was designed to be spacious, well-ventilated, and equipped to support the activities carried out in the laboratory. The laboratory was organized with distinct sections for chemical analysis, primary packaging, and microbiological testing.

The microbiological section was equipped with separate AHUs to supply filtered air to the rooms. Additionally, all processing areas, primary packaging areas, raw material stores, dispensing areas, sampling areas, purified water plant areas, and microbiological testing areas featured self-leveled epoxy flooring, contributing to the facility's clean and controlled environment.

b. Sanitation and Hygiene

The facility followed a cleaning validation procedure to ensure adequate sanitation and hygiene across the environment, personnel, premises, and equipment. It was located in an environment that minimized the risk of contamination to raw materials and products. The cleanliness of the surroundings was maintained at an acceptable level, and access control measures were implemented to regulate the entry of materials and personnel.

Incoming materials were cleaned before being stored in the warehouse, and personnel were required to change gowns and sanitize before entering the production areas. Separate changing rooms for men and women were provided in each workshop, along with lockers for storing clean company garments and street clothes, as well as bins for used clothing.

The facility had clearly defined standard operating procedures (SOPs) for entry and exit to the production area, including pictorial instructions available in the changing rooms. Both primary and secondary changing rooms for men and women were well-equipped with cabinets, crossover benches, shoe covers, and head covers. Cleaning procedures were categorized into Type A and Type B, with disinfectants and detergents managed according to SOPs to prevent microbial contamination.

Microbial and environmental monitoring procedures, with defined alert and action limits, were in place for the production area. Cleaning records were reviewed and SOPs for operating and cleaning procedures.

3. Production

a. Production Line I (Sterile eye drop)

Facility had two mixing tank 750L each and two (2) filling tank 250L each. Process control by QC was assay, appearance, PH, bioburden and production control was temperature, speed, and filter integrity test Records for production of products were maintained in BMR which were verified during the inspection. All In process control reports were recorded in IPC section.

b. Production Line II (Topical semisolid production line (Ointment, cream & Gel))

The dispensing of raw materials, weight was verified by production before preparation of ointment base. This step was followed by addition of active ingredient mixing or homogenization then filling. Before filling the following parameter were monitored particle size, assay, appearance, temperature vacuum, speed of mixing. Critical process parameter under filling stage was filling uniformity, leakage and integrity test and physical appearance.

c. Production Line III (Oral liquid production line)

The production process began with the release of raw materials from the stores, followed by dispensing in the designated area. The materials then underwent preparation, mixing, and/or homogenization then filtration for purification, ensuring their quality. The product was transferred to a storage tank, ready for filling. Highly purified water, which was released and used during the process, met all necessary quality specifications. The final product was then packaged for distribution. Throughout the process, strict quality control measures were maintained to ensure the consistency and safety of the product. Critical process parameters controlled during preparation included temperature, pH, speed, and appearance

d. Production Line IV (Sterile eye ointment line)

Manufacturing began with the dispensing of materials in the designated area, followed by the preparation of the ointment base. The ointment base was then sterilized using a dry heat sterilizer. After sterilization, sterile active ingredients were added, and the mixture underwent further mixing and/or homogenization in a Class B area then filling a Class A area.

The product was then placed in quarantine before being moved to the sterile eye-ointment manufacturing area. Once the finished product was ready, it was stored in the finished product store. Sterile packaging materials were released and used for packing the product, and highly purified water was used throughout the process as required.

Production documents were maintained in the BMR, which were verified during the inspection. Line clearance was completed per SOP, with approval from QA. Critical process parameters controlled during mixing included temperature, pH, speed, and appearance.

e. Production Line V (Non-sterile nasal drops & spray line)

There was no activity at time of inspection. Only primary packaging as explained in the packaging section.

f. Production Line VI (Non-sterile ear drops)

There was no activity at time of inspection. Only primary packaging as explained in the packaging section.

g. Metered dose nasal spray production line

The process began with the release and double-checking of raw materials, followed by preparation, mixing/homogenization, and filtration for purification. After filtration, the product was stored in a tank before being transferred to the filling stage. The Batch Manufacturing Records (BMR) were reviewed, and line clearance was conducted as per SOP with approval from QA before production began. All critical parameters were controlled during preparation.

4. Quality Control

The Quality Control (QC) laboratory handled the testing of raw materials, packaging materials, finished goods, and environmental monitoring samples. The procedure for receiving and testing raw materials was followed, with samples recorded in an active or inactive raw material register. Retained samples were stored in a controlled room, with environmental conditions monitored. Retention samples were kept for one year after expiry, and their management followed procedure in place and were verified and found satisfactory. Analytical procedures and specifications were available for raw materials, packaging materials, and finished goods. The specifications were controlled according to the document control policy.

The facility had a system in place for validating and verifying analytical test procedures. An approved procedure was followed for analytical method verification, ensuring that methods met the requirements. The analytical method validation protocol and reports for analysis of raw materials and finished products were reviewed, confirming that the

method met analytical parameter acceptance criteria and was used for routine QC and stability analysis.

The facility had reference standards for analytical testing, stored in a calibrated refrigerator per the manufacturer's recommendations. The procedure outlined the handling and storage of reference standards. Validity was checked monthly, and the validity reports and confirmed to be valid.

Reagents and volumetric solutions were managed according to approved procedures. The procedures included monitoring hygroscopic reagents, preparation and standardization of solutions, and maintaining records. Set the standardization frequency for volumetric solutions to once a month, with a shelf life of six months for reagents in brown glass bottles and three months for colored reagents in the same bottles.

Analytical worksheets contained adequate information related to the testing performed. Quality assurance officers reviewed the completed analytical data sheets before releasing batches.

Out-of-specification (OOS) results were handled according to procedure in place. The OOS logbook was reviewed and records from 2021 to 2024. One investigation report for products manufactured was reviewed, confirming an OOS due to the assay for the active ingredient being out of range. The investigation identified the root cause as the amount of water added to the bulk product, leading to corrective actions and CAPA closure.

The laboratory-maintained control over glassware, ensuring the use of calibrated and certified Class A volumetric glassware as confirmed by certificates of analysis. Glassware was checked for accuracy, properly labeled, and cleaned as per SOPs. Calibration and cleaning records were maintained.

Some analytical testing was outsourced to qualified laboratories, as per approved procedure. A technical agreement with contract laboratories was in place and still valid, with the contracted laboratory being accredited.

5. Equipment

Equipment and utilities were maintained according to procedure in place. Maintenance and calibration plan were in place and reviewed. It was observed that equipment maintenance was performed as scheduled, such as the maintenance reports which showed that maintenance was completed as indicated on the maintenance labels.

Calibration of instruments was performed according the approved procedures and calibration schedule. Both internal and external calibration services were used and calibration was performed with reference or secondary standards. A maintenance report for sampled for AHU calibration was verified, showing adherence to the procedure. Equipment qualification followed approved procedures with protocols and certificates for equipment available.

6. Purified water System

The water used in the facility was sourced from either the city water supply or a natural well, both of which were approved by Jordanian authorities. Municipal water was chlorinated before being stored in a 3600L tank in the basement. It was then passed through a sand filter and transferred to the water treatment plant on the fourth floor, where it underwent additional filtration through carbon filters and double softeners before being stored in the soft water tank.

From the soft water tank, the water was filtered through a 50µ filter, treated with Sodium Metabisulphite to remove chlorine, and then passed through a double RO system, electrical deionizer, UV lamp, and a final 2µ filter to produce highly purified water. The system had a maximum capacity of 1200L per hour, with a storage tank capacity of 3600L. The water was circulated at temperatures between 15-25°C to prevent microbial growth. The system was operated in compliance with British and European Pharmacopeia specifications for highly purified water.

Online monitoring for flow, pressure, and conductivity was implemented, and records were maintained in a logbook. All materials used in the treatment system were made of SS316L, and collected samples were tested for both chemical and microbiological parameters. Records indicated that the system had operated as expected, and sampling and testing had been conducted according to the schedule, with results consistently within specifications.

7. Heating, Ventilation and Air Conditioning

The facility had a total of 18 AHUs, with each production line having a dedicated AHU. The sterile production line had two AHUs, one for the preparation room and one for the filling room. The operation of AHUs was governed by approved procedure and their maintenance was tracked in the usage logbook. A preventive maintenance plan was in place for all AHUs.

In sterile production areas, there was no air recirculation, while recirculation was limited to non-sterile areas (Class D). The air filtration system included double primary filters, bag filters, and HEPA filters for production areas. The filtered air in cleaning areas maintained positive pressure to prevent contamination, and HEPA filters were installed

in Class B and C areas. Records for the qualification, maintenance, and calibration of critical area such as sterile production areas were reviewed and found satisfactory.

8. Document Review

Generally, the document reviewed indicated that the facility had prepared documents as per prescribed format and its documentation system for the procedures, records, specifications and policies were observed to support quality management and quality assurance activities.

Part 3: Conclusion

The facility was considered to be operating at an acceptable level of compliance with TMDA Guidelines for Good Manufacturing Practices Inspection of Human Medicinal Products Manufacturing Facilities; 1st Edition April, 2023 for three years for production of general pharmaceutical formulations in form of general and cortisone sterile formulations in form of Eye, Ear and Nasal drops, semi solid (Eye ointments and gels); and general and cortisone non-sterile formulations in form of oral liquids (suspension, syrup, solution), external formulation (solution, lotion, suspension, spray); semisolid (ointments, cream, gel and oral gel), nasal/ear drops and nasal spray.

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. Tanzania Medicines and Medical Devices Act, Cap 219.
2. The Tanzania Medicines and Medical Devices (Good Manufacturing Practice Enforcement) Regulation, 2018.
3. The Tanzania Medicines and Medical Devices Authority Guidelines for Good Manufacturing Practices Inspection of Human Medicinal Products Manufacturing Facilities; 1st edition, April 2023.
4. TMDA Good Manufacturing Practices Manual *and SOPs*, Tanzania Medicines and Drugs Authority, Dar-es-Salaam, Tanzania.
5. Amman Pharmaceutical Site Master File SMF QA001 revision 15 effective from 19/2/2014.
6. Amman Pharmaceutical Industries Co., King Abdullah II, Industrial City, Amman 1152, Jordan GMP Inspection Report.
7. TMDA RIMS