LICENSING AND ENFORCEMENT DIVISION

PUBLIC cGMP INSPECTION REPORT OF PHARMACEUTICAL MANUFACTURER:

Name of company: **Troikaa Pharmaceuticals Ltd**

1.0 General information

1.1 Name of Inspected company	**Troikaa Pharmaceuticals Ltd**
1.2 Physical address	Block No. 2019,2022,2023, Village Virochannagar, TA Sanand, Dist Ahmedabad, Gujarat, India - 382 170
1.3 Corporate address	Commerce House – 1, Satya Marg, Bodakdev, Ahmedabad-380 054, Gujarat, India
1.4 Summary of the main activities performed	Manufacture of the following finished pharmaceutical dosage forms: Organogel, Buccal Paste, Ointment, Topical solution and creams, general ampoules and general vials
1.5 Scope of Inspection	Product based inspection to verify compliance with cGMP guidelines for the manufacture of: Organogel, Ointment, Topical solution and creams, general terminally sterilised ampoules and terminally sterilised general vials
1.6 Purpose of Inspection	To ascertain cGMP compliance to support registration of new products and continued registration of products in Zimbabwe
1.7 Inspectors	Ms Martha Mwatseteza - **Lead-inspector** Mr. Sly Mutyavaviri **–Co-inspector**
1.8 Date of Inspection	17th – 19th of February, 2025

2.0 Abbreviations

Abbreviation	Full Form
AHU	Air Handling Unit
CAPA	Corrective and Preventive Action
DPML	Direction de la Pharmacie, du Médicament et des Laboratoires (Ivory Coast)
EM	Environmental Monitoring
FDA	Food and Drug Administration
FTIR	Fourier Transform Infrared Spectroscopy
GC	Gas Chromatography
HPLC	High-Performance Liquid Chromatography
HVAC	Heating, Ventilation, and Air Conditioning
INPRA	National Pharmaceutical Regulatory Agency (Malaysia)
INVIMA	Instituto Nacional de Vigilancia de Medicamentos y Alimentos (Colombia)
LAF	Laminar Air Flow
MAL	Material Air Lock
MCAZ	Medicines Control Authority of Zimbabwe
MOH	Ministry of Health
NDA	National Drug Authority (Uganda)
NVPC	Non-Viable Particle Count
OOS	Out of Specification
PAL	Personnel Air Lock
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PMRA	Pharmacy and Medicines Regulatory Authority (Malawi)
PQR	Product Quality Review
PW	Purified Water
QA	Quality Assurance
QC	Quality Control
RLAF	Reverse Laminar Air Flow
SOP	Standard Operating Procedure
TFDA	Tanzania Food and Drugs Authority
TRS	Technical Report Series
WFI	Water for Injection
WHO	World Health Organization
cGMP	Current Good Manufacturing Practice

3.0 Summary

3.1 Brief summary about the facility

Troikaa Pharmaceuticals Ltd located at Block No. 2019,2022,2023, Village Virochannagar, TA Sanand, Dist Ahmedabad, Gujarat, India - 382 170. The company manufactures Organogel, Ointment, Topical solution and creams, general terminally sterilised ampoules and terminally sterilised general vials.

The Medicines Control Authority of Zimbabwe (MCAZ) Inspectorate audited the blocks manufacturing vials, ampoules and topical solutions. The audit was conducted from the 17th to the 19th of February 2025. The company had been audited by other regulatory bodies as follows:

Country	Agency
India	WHO
Colombia	INVIMA
Malaysia	INPRA
Tanzania	TFDA
Kenya	PPB
Uganda	NDA
Kazakhstan	MOH
Ivory Coast	DPML
Philippines	FDA
Syria	MOH
Malawi	PMRA

3.2 General Information about the Company and the Site

This was a new inspection of the site by the Medicines Control Authority of Zimbabwe (MCAZ) Inspectorate, to support registration of products in Zimbabwe. The inspection was product-based and focused on the products that were intended for the Zimbabwean market, as provided below:

Product	Dosage form	Registration number
Dynapar injection - Diclofenac sodium 75mg/ml injection	Injection(ampoule)	Pending registration

Dynapar QPS -diclofenac diethylamine 4.64% 30ml topical solution	Topical solution	Pending registration
Propofol 1% W/V BP injection	Injection (vial)	Pending registration

The first day activities comprised of an introductory meeting in which the MCAZ Inspectorate and the Troikaa team introduced themselves. This was followed by a projected Troikaa Company power-point presentation. Thereafter the scope of the inspection was defined, both parties agreed on the blocks to be inspected. Immediately after, extensive document review commenced. Later in the day a walk-through inspection was conducted, for the raw material warehouse and the production block for the injectables (ampoules).

Second day activities encompassed further document review and the inspection of the utilities block (Water Purification and HVAC system) and the external preparation block (Organogel, Ointment, Topical solution and creams). The third day comprised of further document review, an inspection of the quality control laboratories chemistry section and the microbiology section, and the vial block. The inspectors then held an inspectors' meeting in which findings from the inspection were discussed and there was consensus on the inspection findings.

The inspection was conducted with reference to and in accordance with the WHO Good Manufacturing Practices detailed in the Technical Report Series 986, Annex 2 of 2014, among other relevant current guidelines. The inspection was conducted in an open and cooperative atmosphere.

3.3 Areas inspected

- **Quality Management**: Product Quality Review (PQR), Quality Risk Management, Deviation control, finished product and starting material batch release, Contract agreements and Supplier approval.
- **Materials Management**: Receipt, handling, quarantine, sampling, release, reject, temperature (and humidity) monitoring and dispensing.
- **Good Practices in Production**: Production areas, production equipment, documentation and instructions, sanitation cleaning and maintenance, batch records, calibration, contamination control, in process controls.
- **Quality Control**: Review of test procedures and specifications.
- **Utilities**: HVAC, Purified Water,
- **Environmental Monitoring**: EM Program
- **Equipment qualification** and preventive maintenance

3.4 Utilities

a. Water Purification system
b. HVAC system
c. Compressed air system

3.5 Documents reviewed

As listed in the final inspection

3.6 System Summaries

Pharmaceutical Quality System

Product Quality review (PQR)

SOP for Product Quality review was submitted for review. The PQRs were being erected in line with the current WHO TRS guidelines. The role of preparing the PQR was of the Quality Assurance (QA) officer, the subsequent roles of the other teams including Production and QC were explained. The preparation of PQR reports was on an annual basis. PQRs of some of the products were submitted for review. The starting materials, in process quality control and critical quality attributes were being reviewed. The statistical evaluations were presented. Examples of PQRs were submitted for review to ascertain the implementation of the PQR SOP.

Complaints

The SOP for complaints handling was submitted for review. There was provision of categorization of the complaints. Clearly defined procedures from receipt to root cause identification with CAPA proposals were available. The log of complaints handling was submitted for review. All the complaints were being adequately reviewed with all CAPAs being scientifically plausible.

Deviations

The SOP for handling of deviations was submitted for review. The deviations were classified as minor and major. The log of deviations was submitted for review. Root cause identification was being done using the relevant SOPs. Examples of deviations were reviewed to demonstrate the implementation of the procedure.

Change Control

The Change Management Process SOP was submitted for review. There was provision of a multi-disciplinary approach for change management. The SOP provided for change initiation,

impact assessment, execution and effectiveness evaluation. The log of changes was reviewed. Quality impacting changes were reviewed and these were satisfactory.

Product Recall

SOP for product recalls were submitted for review. These were either voluntary or initiated by the regulatory authorities. There was provision of classification of the recalls according to the level of inherent risk. The SOP provided for execution of mock recalls to evaluate the effectiveness of the SOP for recalls. The mock recalls were evaluated and these were acceptable.

Vendor Qualification

SOP for vendor management was submitted for review. There was provision of pre audit questionnaire evaluation. Post the initial evaluation, there was provision of onsite audits and then provision of pilot batches for evaluation. The approved vendor list was submitted for review. The compliance state of the different suppliers was verified. There was provision of ongoing vendor monitoring or evaluation.

Stability Studies

The SOP for stability monitoring was submitted for review. The ongoing stability program was evaluated. The protocols for the products under review were evaluated and were satisfactory.

Self-Inspection

The SOP for self inspection was submitted for review. There was provision of an inspection calendar. The approach to qualification of the internal auditors was specified. The SOP provided for audit observations classification, CAPA handling and effectiveness monitoring. The inspections observations and the subsequent CAPAs were recorded in the log of CAPA according to the SOP for handling CAPAs.

Training

The SOP for training was provided for review. This provided for onboard training, continuous training and refresher trainings. The divisional training calendars were provided, and these were being adhered to. There was provision of training effectiveness verification.

Quality Risk Management

The SOP for risk assessment was submitted for review. This provided for risk identification, risk rating and evaluation, risk mitigation and risk review. The examples of risk evaluation tools used were provided. Risk principles were being applied throughout the pharmaceutical

quality system. Examples of executed risk assessments were evaluated to show application of the SOP.

Materials Management

There was provision of SOP for materials receipt. All the key components to support the supply chain traceability were provided. There was provision of approved vendor lists which were being verified at the time of importation. Quarantine, sampling and dispensing areas were provided.

Utilities and Equipment
Preventive maintenance

The SOP for preventative maintenance was provided for review. The preventative maintenance calendar was provided. The equipment was being maintained according to the calendar.

Air Handling Units (AHUs)
The AHUs were inspected. There was adequate level of filtration. Failure safe mechanisms were in place to ensure provision of the adequate cleanroom environments. Appropriate building management systems were in place.

Purified Water System (PW)

The P and ID diagrams for the water system was provided. The source of water was in a state of control. All the SOPs for generation, distribution and challenge tests were provided. The water trends were submitted for review and these were acceptable.

Quality Control tour
The QC laboratory was inspected. There was provision of all the key equipment such as HPLCs, GCs, FTIRs. Laboratory managements system were in place and the approach to sample receipt, sample allocation, analyses and column management was satisfactory.

Out of specification (OOS) handling

SOP for handling of out of specifications was submitted. A flow diagram showing the stepwise phase investigation was presented. The SOP had responsibilities for all the key personnel, starting with the analyst, Quality Control (QC) in charge and the reviewers. Appropriate root cause identification tools were being used. The log of OOS was submitted for review and all the OOS had been reviewed with appropriate CAPA suggested.

HPLC

An adequate number of HPLCs was provided. The SOP for good chromatographic practices was submitted for review. Audit trail SOPs and worksheets were reviewed. Appropriate data management procedures were in place.

FTIR

The SOP for operation of the FTIR were in place. These were adequately calibrated. Records of utilization were verified and these were acceptable

Batch manufacturing Records

BMR records were submitted for review. The SOP for batch productions were submitted for review. There was adequate control of the master production documents. The dispensing section of the BMR was reviewed and was satisfactory. The compounding stage was verified including the cleaning and sterilisation of the components was reviewed. Appropriate environment control was being done. The line assembly line clearance was provided and was satisfactory. The Filtration stage was reviewed. The nitrogen handling procedures were submitted and were acceptable.

Facility tour

There was provision of a vial line and two ampoule lines.

Vial line

The vial de-cartonating, washing, depyrogenation, filling, stoppering to crimping to inspection was inspected. The appropriate environments were provided. all the appropriate critical process parameters were provided.

Ampoules

The ampoules decartonating, washing, depyrogenation, filling and sealing stations were reviewed. All critical stages were SOP driven.

Filling area.

The filling area was provided. this was in a good state of repair. All the environment monitoring was being done and aseptic techniques were being executed.

Ampoule inspection and packing line

The SOP for automatic ampoule inspection was provided for review. The camera challenge tests were submitted for review. The packing lines were reviewed and were satisfactory.

Disinfectant handling

SOP for preparation, filtration and usage of disinfectant or surfactant solution was submitted for review. Disinfectants were adequately prepared, filtered and packed. Log books for preparation were verified.

Environment Monitoring (EM)

The SOP for environmental monitoring was submitted for review. The approach to non viable particle counts and viable particle counts was specified. for the viable this included passive, active and contact sampling. The EM trend reports for 2024 was submitted for review.

Visual Inspection and trend reports

The SOP for visual inspection trends was submitted for review. There was categorisation of the defects into critical, major and minor.

Steam steriliser

The steam steriliser was adequately qualified and there was provision for continuous monitoring of key parameters such as temperature.

Facility tour (External Preparations)

The warehouse was inspected. There was provision of receipt area, quarantine area and approved raw materials store. The materials were being adequately handled as provided by the SOPs.

Dispensaries

Two dispensary areas which were kept in a good state of repair were submitted. The approach to the RLAF cleaning and handling was specified and this was satisfactory.

Wash area

An equipment wash area was provided**.** There was provision of dirty, washing, drying and clean areas, separated by pressure differentials.

Manufacturing cubicles

The manufacturing area 2, was inspected. This was in a good state of repair. The equipment had been qualified and status stickers were provided.

Compounding

The compounding area was provided. The critical process parameters were being monitored.

Liquid manufacturing area 2

A liquid manufacturing area was provided. The SOP for operation and cleaning of the tanks were submitted for review and these were satisfactory.

Gel manufacturing area

There was a gel manufacturing area which was provided. There was provision of personnel airlock (PAL) and material air lock (MAL) into the area.

Ointment manufacturing area and gel manufacturing

The area was inspected. There was provision of three compounding tanks. These were all in a good state of maintenance. The SOPs for operation and cleaning were submitted for review.

Quarantine area

There was provision of a liquids quarantine area. The liquids quarantine area had a log book.

Glass bottle washing

There was provision of bottle washing. The SOP for bottle washing was submitted for review. Critical parameters were being monitored.

Filling area: cream and ointments and gel and paste

Filling area was provided and proper line clearance was being provided.

Filling of external liquid

The external liquids filling area was inspecting. The SOPs for line clearance and operation were submitted during the inspection.

Facility tour

Ampoule filling line

The ampoule filling line setup was inspected and this was satisfactory. All the aseptic techniques were being followed

Vial line inspection

There was provision of vial inspection, washing, depyrogenation, and filling. The products were all terminally sterilised. The line was in a good state of repair.

Vial inspection

There was provision of a 100% manual vial inspection. The vial inspection SOP was provided.

Quality Control

Microbiology

The microbiology section was inspected. The key areas such the Bacterial endotoxin test area, sterility test areas were inspected. An isolator was being used for sterility testing and the disinfectant qualification reports were submitted for review. The qualification of the isolator was submitted for review.

Incubators

Incubators were provided and these were mapped and adequate monitoring was being done. Failure safe mechanisms were provided.

WFI Testing

SOP for water sampling and testing was submitted for review. The media handling procedures and the growth promotion procedures were reviewed and were satisfactory. The monthly reports were verified against the schedule and were satisfactory.

Colon counting

The SOP for cleaning and operation of colon counter was submitted for review. There was provision of doer and checker.

Qualifications and Validations

Area Classifications

The areas schematic diagrams were submitted for review. There was provision of individual airlocks and MAL for the processing cubicles. The SOP for qualification, requalification and periodic monitoring of HVAC system, RLAF/LAF and dynamic pass box was reviewed. The validations were protocol driven. The frequency of requalification were submitted.

The PQ report for the Terminal steriliser was submitted

Depyrogenation tunnel Qualification

There was provision of a once in a year requalification and the filter integrity twice in a year. Key parameters such as non-viable particle counts (NVPC), HEPA leakage, BET test, Velocity tests, air flow visualisations amongst others had been executed.

Cleaning Validation

The SOP for cleaning validation program was submitted for review. The approach to worst case product determination was provided. The executed cleaning validations were reviewed. The validated parameters were transferred to the SOPs.

4.0 Conclusion

Based on the areas inspected, the people met, and the documents reviewed including the observations listed in the Inspection Report **Troikaa Pharmaceuticals Ltd** located at **Block No. 2019,2022,2023, Village Virochannagar, TA Sanand, Dist Ahmedabad, Gujarat, India - 382 170** was considered to be operating at an acceptable level of compliance with WHO TRS cGMP guidelines for the manufacture of the following:

Dosage form	**Compliance**
General Organogel, General Ointment, and general topical solution and creams	Acceptable
General terminally sterilized ampoules and General terminally sterilized vials	Acceptable

All the non-compliances observed during the inspection listed in the full report were addressed by the manufacturer to a satisfactory level prior to the publication of the MCAZ PIR

The site will be reinspected **3 years** from the date of the last inspection in line with the risk based reinspection frequency determination.

5.0 References

1. WHO good manufacturing practices for pharmaceutical products: main principles. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Eight Report* Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2 http://www.who.int/medicines/publications/pharmprep/en/index.html

2. WHO guidelines on good manufacturing practices for heating, ventilation and air-conditioning systems for non-sterile pharmaceutical dosage forms. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8, https://www.who.int/publications/m/item/Annex-8-trs-1010
3. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3 https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/production/trs1019-annex3-gmp-validation.pdf?sfvrsn=9440a5c_0&download=true
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5. WHO good practices for pharmaceutical microbiology laboratories. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report*. Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2 http://www.who.int/medicines/publications/pharmprep/en/index.html

6. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. *WHO Expert Committee on specifications for pharmaceutical preparations*. *Forty-third report.* Geneva, World Health Organization, 2009. (WHO Technical Report Series, No. 953), Annex 2 http://www.who.int/medicines/publications/pharmprep/en/index.html

7. WHO guidelines on quality risk management. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report* Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2 http://www.who.int/medicines/publications/pharmprep/en/index.html

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http://www.who.int/medicines/publications/pharmprep/en/index.html

9. WHO Expert Committee on Specifications for Pharmaceutical Preparations. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty Ninth Report* Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4
http://www.who.int/medicines/publications/pharmprep/en/index.html