LICENSING AND ENFORCEMENT DIVISION

PUBLIC cGMP INSPECTION REPORT OF PHARMACEUTICAL MANUFACTURER:

Name of Company: Brooks Steriscience (Pvt) Ltd

1.0 General information

1.1 Name of Inspected company	Brooks Steriscience (Pvt) Ltd
1.2 Physical address	Survey No.61& 62, Village-Manglej, Nareshwar Road, Taluka-Karjan, District-Vadodara 391243, Gujarat, India. Tel.: 91- 2666 – 235500
1.3 Corporate address	201, "The Summit Business Bay", Behind Guru Nanak Petrol Pump, Off. Andheri Kurla Road, Andheri East, Mumbai-400093 Phone: 022 69073100.
1.4 Summary of the main activities performed	Manufacture of Small Volume Parenterals – Dry Powders for Injection (Vials) and Lyophilized Injections (Vials).
1.5 Scope of Inspection	Product based inspection to verify compliance to cGMP guidelines for the Manufacture of Small Volume Parenterals – Dry Powders for Injection (Vials), Line I.
1.6 Purpose of Inspection	To ascertain cGMP compliance for the products which have been submitted for registration with the Medicines Control Authority of Zimbabwe (MCAZ)
1.7 Inspectors	Mr. Tendai Samkange – **Lead Inspector** Mr. Clive S. Kamhoti – **Co-Inspector**
1.8 Date of Inspection	20^{th} to 21^{st} March, 2025

2.0 Abbreviations List

Abbreviation	Expanded Form
AHU	Air Handling Unit
API	Active Pharmaceutical Ingredient
EDI	Electrode Deionization
EM	Environmental Monitoring
HVAC	Heating, Ventilation, and Air Conditioning
ISO	International Organization for Standardization
LAF	Laminar Air Flow
MCAZ	Medicines Control Authority of Zimbabwe
NLT	Not Less Than
NVPC	Non-Viable Particle Count
OOS	Out of Specification
PIR	Public Inspection Report
PM	Preventive Maintenance
PQR	Product Quality Review
PV	Process Validation
QC	Quality Control
SOP	Standard Operating Procedure
TRS	Technical Report Series
WHO	World Health Organization

3.0 Summary

3.1 Brief summary about the facility

Brooks Steriscience (Pvt) Ltd located at Survey No.61& 62, Village-Manglej, Nareshwar Road, Taluka Karjan, District-Vadodara 391243, Gujarat, India, was inspected. The site manufactures Sterile Dry Powders for Solution for Injection (vials) and Lyophilized Injections (vials).

The Medicines Control Authority of Zimbabwe (MCAZ) Inspectorate audited the block manufacturing Sterile Dry Powders for Solution for Injection packaged in vials. The audit was conducted from the 20th to 21st of March 2025. The company had been audited by other regulatory bodies as listed in the table below.

Country	Agency
USA	USFDA
Croatia	HALMED (EU-GMP)
Brazil	ANVISA
Ukraine	Ministry of Health of Ukraine
Kenya	PPB
India	CDSCO – WHO GMP
Sudan	Ministry of Health

3.2 General Information about the Company and the Site

This was an initial 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 listed below:

Product	Dosage Form	Registration number
Meropenem (As Trihydrate), 500mg	Sterile Dry Powder for Solution for Injection	Pending Registration
Meropenem (As Trihydrate), 1000mg	Sterile Dry Powder for Solution for Injection	Pending Registration
Imipenem/Cilastatin (500mg/500mg)	Sterile Dry Powder for Solution for Injection	Pending Registration

The inspection was conducted over two (2) days. The inspection was conducted with reference to and in accordance with the World Health Organization (WHO) Good Manufacturing Practices guidelines detailed in the Technical Report Series (TRS) 986 Annex 2 and TRS 1044 Annex 2, among other relevant current guidelines. The inspection was conducted in an open and cooperative atmosphere.

3.3 Areas inspected *(Not exhaustive)*

- **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, Compressed Air system
- **Environmental Monitoring**: EM programme
- **Equipment qualification** and preventive maintenance

3.4 Utilities

a. Water Purification system

b. HVAC system
c. Compressed Air System

3.5 Documentation reviewed *(Not exhaustive)*

As stated in the final report

4.0 System Summaries

Walk-through Inspection
The walk-through inspection of production areas followed the logical flow of materials, that is from receipt of raw materials to the final packaging and storage of the finished pharmaceutical products.

Warehouse
There was a weather-protected materials receiving area at the entrance and provisions for rodent and pest control. The materials receiving procedure was reviewed on spot. There was a materials receiving checklist which captured adequate details. There was a provision for recording both the material manufacturer's name and supplier's name for supply chain traceability. Materials were managed through a validated electronic system. There were cold storage facilities in the warehouse for storage of temperature and time sensitive materials.

Production Area Tour (Line 1)
The production area was located on the Ground floor, the inspection followed the production in line 1 which started with glass vial decartoning and inspection area, the environment in this room was classified as Grade D. There was provision for hourly breaks for visual inspectors, and the defects library was displayed in the decartoning area. Inspected glass vials would be transferred into a Grade C washing and depyrogenation area through a conveyer belt.
The washed vials would be conveyed through a depyrogenation tunnel for not less than three (3) minutes at a tunnel temperature of NLT 300°C. There was continuous recording of the depyrogenation parameters, and these would be reviewed as part of the batch release review.
There was provision of environmental monitoring during filling, where four non-viable particle counts (NVPC) probes were placed in different locations including: at the turn table, filling nozzles area, stoppering station and under the extended laminar air flow (LAF) of the O-RABS.
There was provision of passive viable particle monitoring in both Grade A and B areas of the aseptic filling room.

Batch Manufacturing Records
The batch manufacturing records for products under the scope of the inspection were reviewed. Relevant batch details were stated. The batch was manufactured in September 2024 and had a shelf-life of two years (24 months). The yield was within the validated limit. There was

provision for recording interventions. There was provision for clarity testing and leak testing after vial crimping and sealing.

Product Quality Review (PQR)
The relevant procedure for conducting product quality reviews was reviewed. The responsibilities for people involved in the generation of PQR were provided. PQRs were to be compiled every year, within forty five (45) days of the last day of the period under review. The parameters reviewed in the PQR were in-line with those stated in WHO TRS 986 Annex 2.

Complaints handling
The SOP for handling market complaints was also reviewed. There was a clear process on the classification and investigation of critical, major and minor complaints. The procedure was clear on the number of retention samples to be investigated for each complaint type.

Material Management
The review of starting materials included reviewing the vendor qualification status. There was use of different material codes for APIs coming from different vendors. The relevant procedure for vendor management was reviewed and found to be satisfactory. The procedure covered the handling of all types of APIs, primary packaging and secondary packaging materials.

Investigation of Out-of-Specification Results
The procedure for handling and investigating out-of-specification (OOS) results obtained in the Quality Control laboratory was reviewed and considered satisfactory. There was a phased approach to OOS investigations. The procedure allowed for investigations to be conducted in two phases – Phase I and Phase II. There was evidence of root cause investigation during OOS investigations.

Stability Monitoring
The procedure for sampling, handling and analysis of stability study samples was reviewed and found to be satisfactory. There were provisions for monitoring stability of products under accelerated stability, Zone II, Zone IVa and Zone IVb conditions.

Aseptic Process Simulation
The procedure for aseptic process simulation was reviewed and found to be satisfactory. Media Fill Studies were conducted on a six-monthly basis on each production line. There was provision for recording interventions, pre-incubation visual inspection, post incubation growth promotion testing and post incubation container closure system integrity tests.

Water System
The purified water and water for injection plants were inspected. Purification of water was

achieved through reverse osmosis and electrode deionization (EDI), whereas WFI was generated through distillation.

Compressed Air
The compressed air generating systems were inspected. Compressed air would pass through a series of filters before use.

Nitrogen Gas
The Nitrogen generation plant was inspected and found to be satisfactory. There was provision for Quality Control testing of processing gases.

Process Validation
The relevant procedure for process validation (PV) was reviewed. The approach to PV followed the current approach where process design, process qualification and continued process verification would be executed. Evidence of executing these stages was provided.

HVAC Qualification
The relevant SOP for AHU qualifications was reviewed. The frequency of requalification for the different room cleanliness levels was defined. The parameters considered during performance requalification were as per the ISO 14644 guidelines.

Equipment Qualification for Steam Sterilizer
The periodic performance qualification for Steam Sterilizer was carried out at stipulated intervals. Tests considered included: non-condensable gas test, super heat test and dryness value test, vacuum leak test, Bowie-Dick test and the heat distribution and penetration studies.

Quality Control Laboratory
The QC laboratory was inspected. The inspection was done following the logical flow of samples from receipt to final release of analysis results. The relevant procedure for receipt and allocation of samples for analysis was reviewed and found satisfactory.

Environmental Monitoring
There was a robust microbiological environment monitoring program in place. The procedure for environmental monitoring was reviewed and found satisfactory. Identification of microbes was done in a satisfactory manner.

Reference Cultures
The laboratory had adequate storage facilities for reference and working cultures used for microbiology analysis. The procedure for microbial cultures management was reviewed and found to be satisfactory.

Preventative maintenance program

The relevant procedure for PM was reviewed. The preventative maintenance planner was informed by risk principles such as criticality of equipment.

5.0 Observations

As stated in the final report

6.0 Conclusion

Based on the areas inspected, the people met, and the documents reviewed including the observations listed in the Inspection Report, **Brooks Steriscience (Pvt) Ltd,** located at **Survey No.61& 62, Village-Manglej, Nareshwar Road, Taluka Karjan, District-Vadodara 391243, Gujarat, India** was considered to be operating at an acceptable level of compliance with cGMP guidelines for the manufacture of Sterile Dry Powders for Solution for Injection packaged in vials.

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 **4 years** from the date of the last inspection in line with the risk-based reinspection frequency determination.

7.0 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

4. Supplementary guidelines on good manufacturing practices: validation. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report*. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4 http://www.who.int/medicines/publications/pharmprep/en/index.html

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

8. WHO Expert Committee on Specifications for Pharmaceutical Preparations. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty Ninth Report* Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 3 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