

LICENSING AND ENFORCEMENT DIVISION

FINAL cGMP INSPECTION REPORT OF PHARMACEUTICAL MANUFACTURER:

Cisen Pharmaceutical Co. Ltd

1.0 General information

1.1 Name of Inspected company	Cisen Pharmaceutical Co. Ltd
1.2 Physical address	Hai Chuan Road, Jining High & New Technology Industries Development Zone, Jining city, Shandong
1.3 Corporate address	No.16, Tongji Road, Jining High & New Technology Industries Development Zone, Jining City, Shandong
1.4 Summary of the main activities performed	Manufacture of small volume parenteral solutions, (glass ampoules) and large volume parenterals (Glass bottle and PP bottle)
1.5 Scope of Inspection	Product based inspection to verify compliance to cGMP guidelines for the manufacture small volume parenteral solutions, (glass ampoules) and large volume parentals (Glass bottle and PP bottle)
1.6 Purpose of Inspection	To ascertain cGMP compliance for the products which are currently under registration with the MCAZ.
1.7 Inspectors	Martha Mwatseteza – Lead Inspector Onias Hove- Co-Inspector
1.8 Date of Inspection	24 th , 25 th , 26 th July 2025

2.0 Abbreviations List

Abbreviation	Expanded Form
AHU	Air Handling Unit
BMR	Batch Manufacturing Record

BPR	Batch Processing Record
CV	Cleaning Validation
EM	Environmental Monitoring
FPP	Finished Pharmaceutical Product
HPLC	High-Performance Liquid Chromatography
HVAC	Heating, Ventilation, and Air Conditioning
MACO	Maximum Allowable Carry Over
MCAZ	Medicines Control Authority of Zimbabwe
PDE	Permitted Daily Exposure
PQ	Performance Qualification
PQR	Product Quality Review
QA	Quality Assurance
SOP	Standard Operating Procedure
TD	Therapeutic Dose
TRS	Technical Report Series
WHO	World Health Organization

3.0 Summary

3.1 Summary about the facility.

This was product-based inspection to verify compliance to cGMP guidelines for the manufacture of small volume parenteral solutions, (glass ampoules) and large volume parentals (Glass bottle and PP bottle). The inspection, which included a facility tour and document review, was conducted over a three-day period, during which the operating production lines were observed and reviewed.

This inspection was conducted with reference and in accordance with the World Health Organization, mainly Technical Report Series 986, 2014; (TRS 986), annex 4, Technical Report Series, 961 (2011), annex 2 and Technical Report Series 970 (2012), Annex 2 and Technical Report Series 1044, Annex 2 on GMP for sterile products

3.2 General Information about the Company and Site

Cisen Pharmaceutical Co. Ltd is located at Haichuan Road, Jining High-tech Zone. The company has three manufacturing workshops namely 207, 201 and 202. 207 is used for the manufacture of large volume parenterals (polypropylene infusion bottles). The 201 workshop is used for the production of large volume parenteral (glass infusion bottles). 202 was for the manufacture of glass ampoules.

Regulatory Compliance History

This was an initial inspection of the manufacturer by the Medicines Control Authority of Zimbabwe.

3.3 Areas inspected (*Not exhaustive*)

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- **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

3.5 Documentation reviewed (*Not exhaustive*)

As listed in the final inspection report.

4.0 Summary of Systems

Material management

The facility tour included the inspection of the material storage warehouse, the production of paracetamol infusion in line 201, the production of gentamycin ampoules in line 202 and the production of water for injection in line 207.

Sampling area

The sampling area was inspected and found generally satisfactory.

Production facility tour (Block 207/208 PP bottle)

The production tour focused on aseptic procedures and conduct.

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Pharmaceutical Quality Systems

Product Quality Review (PQR)

The approach to conduction of annual product quality reviews (APQR) and compilations was evaluated and determined to be generally satisfactory.

Vendor Qualification

The approach to vendor qualification was assessed by analysing relevant SOPs and reports. It was deemed generally satisfactory.

Self-Inspections

An analysis of the relevant SOPs and other documents confirmed that the approach to self-inspections was generally satisfactory.

Training

The training program was reviewed and found generally satisfactory.

Product Recall.

The standard operating procedure and recall reports for product recalls was submitted for review and found to be generally satisfactory.

Complaints

The standard operating procedure for handling complaints, as well as the related documentation, were reviewed and judged to be generally adequate.

Deviations Control and Change

Deviation management SOP was submitted for review and found generally satisfactory.

Document Control

The standard operating procedure for document control was submitted for evaluation and determined to be generally satisfactory.

Stability Program

The technique to stability monitoring was assessed and determined to be generally satisfactory.

Product Release Management

The approach to product release was assessed and determined to be generally satisfactory.

Water system

Approved schematic diagrams and parameters for the water systems were reviewed. These were within the specifications.

HVAC

An inspection was conducted on the HVAC system, which encompassed the pressure monitoring gauges, filters amongst other components and associated maintenance records. Additionally, the alarm systems were reviewed. These were found to be satisfactory.

Batch manufacturing records

The batch manufacturing issuance procedure and completed batch manufacturing records were reviewed. They were generally satisfactory.

Process validation (PV)

The methodology for process validation was reviewed for adequacy and compliance. It was found to be satisfactory.

Cleaning validation

An evaluation of the facility's cleaning validation approach was conducted. It was found to be satisfactory.

Clean in place (CIP) and sterilisation in place (SIP) for the manufacturing vessels

An evaluation was conducted on the CIP/SIP provisions for the bulk manufacturing vessels and filling lines. These were found to be generally satisfactory **Sterilization**

The sterilization procedures were reviewed for adequacy and compliance. These were generally acceptable.

Performance Qualification of the Liquid Sterilizer

The re-qualification report for the double-door liquid sterilizer was submitted for review. It was found to be generally satisfactory.

AHU qualification for the filling line (II) Block 202

The team presented the performance qualification for the injectable section's filling area, which was subsequently reviewed. This was found to be generally satisfactory.

Qualification of the Depyrogenation tunnel equipment number 202-008

The qualification of the depyrogenation tunnel was reviewed. It was found to be generally satisfactory.

Environmental Monitoring

The environmental monitoring program and its associated SOPs were assessed. These were found to be generally satisfactory.

Quality Control Tour

During the quality control tour, the samples receipt area was inspected. The procedure for work allotment by the QC Supervisor or their designate was reviewed, along with the approach to analyst qualification, equipment calibration and qualification. The SOP for data backup was also examined. **HPLC**

The approach to HPLC data management and column management was requested for review. These were deemed to be satisfactory.

Sterility testing

The sterility testing procedures and relative documents were reviewed. These were found to be generally satisfactory.

Nitrogen testing

The re-qualification protocol for the nitrogen distribution system was submitted for review. It was found to be generally satisfactory.

Garment qualification

The approach to garment qualification was evaluated. It was found to be generally satisfactory.

Disinfectant qualification The approach to disinfectant qualification and the disinfection rotation matrix was reviewed.

Media Fill

The media fill validation protocol and report were reviewed, and the GPT test results were examined. These were generally acceptable as they were within the specified limits.

5.0 Conclusion

Based on the areas inspected, the people met, and the documents reviewed including the observations listed in the Inspection Report, Cisen Pharmaceutical Co. Ltd, located at Hai Chuan Road, Jining High & New Technology Industries Development Zone, Jining city, Shandong was operating at a level of compliance for the manufacture of small volume parenteral solutions, (glass ampoules) and large volume parenteral solutions (Glass bottle and PP bottle). 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 MCAZ risk-based reinspection frequency determination.

6.0 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 Good Manufacturing Practices: water for pharmaceutical use. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-six Report*. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2
<http://www.who.int/medicines/publications/pharmprep/en/index.html>
 3. 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, 2011 (WHO Technical Report Series, No. 961), Annex 5, Annex 9
<http://www.who.int/medicines/publications/pharmprep/en/index.html>
 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*
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Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4

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

10. WHO Expert Committee on Specifications for Pharmaceutical Preparations. *Forty-fourth report of the WHO Expert Committee on specifications for pharmaceutical preparations*, World Health Organization, 2010 (WHO Technical Report Series 957, 2010), Annex 1
<http://www.who.int/medicines/publications/pharmprep/en/index.html>