

LICENSING AND ENFORCEMENT DIVISION

PUBLIC cGMP INSPECTION REPORT OF PHARMACEUTICAL MANUFACTURER:

Sinovac Biotech Co. Ltd - Changping

1.0 General information

1.1 Name of Inspected company	Sinovac Biotech Co. Ltd-Changping
1.2 Physical address	No. 15, Zhi Tong Road, Changping Science Park, Changping District Beijing P. R. China
1.3 Corporate address	No. 39, Shangdi Xi Road, Haidian District Beijing, P. R. China
1.4 Summary of the main activities performed	Manufacture of Biologics
1.5 Scope of Inspection	Product- based inspection to verify compliance to cGMP guidelines for the manufacture of Biologics.
1.6 Purpose of Inspection	To ascertain cGMP compliance for the products which have been submitted and those yet to be for registration with the Medicines Control Authority of Zimbabwe (MCAZ).
1.7 Inspectors	Mr. Tendai Samkange – Lead Inspector Mr. Shamiso C. Shambira- Co-inspector
1.8 Date of Inspection	30 th June – 4 th June, 2025

2.0 Abbreviations List

Abbreviation	Meaning
APQR	Annual Product Quality Review
ATCC	American Type Culture Collection
BMR	Batch Manufacturing Record
BMS	Building Management System
CAPA	Corrective and Preventive Action
CCS	Container Closure System
cGMP	Current Good Manufacturing Practice
CNC	Controlled Non-Classified Area
COA	Certificate of Analysis
EMS	Environmental Monitoring System
EV71	Enterovirus Type 71

FPP	Finished Pharmaceutical Product
GMP	Good Manufacturing Practice
GPT	Growth Promotion Test
HEPA	High Efficiency Particulate Air
HVAC	Heating, Ventilation and Air Conditioning
ICP-MS	Inductively Coupled Plasma Mass Spectrometry
ICP-OES	Inductively Coupled Plasma Optical Emission Spectrometry
LAF	Laminar Airflow
LIMS	Laboratory Information Management System
MCAZ	Medicines Control Authority of Zimbabwe
MEM	Minimum Essential Medium
NVPC	Non-Viable Particle Count
PBS	Phosphate Buffered Saline
PDE	Permitted Daily Exposure
PFS	Pre-Filled Syringe
PLC	Programmable Logic Controller
PQ	Performance Qualification
QA	Quality Assurance
QC	Quality Control
QIV	Quadrivalent Influenza Vaccine
RA	Regulatory Affairs
RO	Reverse Osmosis
SOP	Standard Operating Procedure
TIV	Trivalent Influenza Vaccine
TOC	Total Organic Carbon
TRS	Technical Report Series
TSA	Tryptic Soy Agar
VHP	Vaporized Hydrogen Peroxide
WFI	Water for Injection
WHO	World Health Organization

3.0 Summary

3.1 Brief summary about the facility

Sinovac Biotech Co. Ltd – Changping, established in 2001, is located in the Changping Science Park, Beijing. The company is a biological high-tech subsidiary of Sinovac Biotech Ltd, operating three industrial bases (Haidian, Changping, Daxing). The Changping site includes production workshops for bulk and finished products, including Enterovirus Type 71 Vaccine (Vero Cell), Inactivated (EV71), Poliomyelitis Vaccine (Vero Cell), Inactivated (IPV), and formulation/filling/packaging lines.

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 product(s) that were intended for the Zimbabwean market, with registration statuses at the time of the inspection as listed below.

Product	Strength	Registration status
23-Valent Pneumococcal Polysaccharide vaccine, (PnuPreve 23)	0.5ml/vial solution for injection	Under evaluation for registration
Hepatitis A Vaccine (Human Diploid cell), (Healive)	Inactivated 500U/0.5ml/dose for adult use, suspension for injection	Under evaluation for registration
Hepatitis A Vaccine (Human Diploid cell)	Inactivated 500U/0.5ml/dose	Under evaluation for registration
Enterovirus 71 Vaccine, (inactivated), (Inlive)	480IU/0.5ml suspension for intramuscular injection	Under evaluation for registration
Influenza vaccine (Split virion), inactivated, (Anflu)	0.5ml pre-filled syringe, suspension for injection	Under evaluation for registration
Influenza vaccine (Split virion), inactivated, Quadrivalent	0.5ml pre-filled syringe, suspension for injection	Under evaluation for registration

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,
- **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 Systems Summary

Pharmaceutical Quality System

A documented system for quality assurance was established, with procedures covering key quality elements in place. The Quality Department was divided into QA and QC and was separate from the Production Department. Operations were specified in written form.

Annual Product Quality Review (APQR): The company had in place a procedure for performing product quality reviews (SOP BJ-SMP-10-015). APQRs are prepared annually within three months after production verification. The APQR for Enterovirus Type 71 (EV71) Inactivated Vaccine (Vero Cells) for 2024 was reviewed and found to include review of cell bank and virus seed lot information, utility trends, and batch data.

Quality Risk Management: The SOP for environmental monitoring included a risk assessment approach for selection of high-risk sampling points. A risk assessment report for clean area environmental monitoring (BJ-RA-20240084) was available, identifying high-risk areas based on frequency of use, personnel flow, and cleaning difficulty.

Deviations and CAPA: A system for handling deviations and implementing CAPA was in place.

Change Control: Change control procedures were documented and a respective register was available.

Product Release: Product release was managed by QA.

The deficiencies identified in this section have been adequately addressed and will be verified during future inspections.

Good Manufacturing Practices for Pharmaceutical Products

Good manufacturing practices were generally implemented. Necessary human and physical resources, including adequate premises, equipment, and utilities, were provided for the current operational level of biologics manufacturing activities. The manufacturing processes followed procedures as defined and documented in the batch manufacturing records. The personnel were appropriately qualified and training was conducted.

Batch manufacturing records for EV71 vaccine bulk and Quadrivalent Influenza Vaccine final product were reviewed and showed defined process parameters, including cell culture conditions, virus inoculation, harvesting, inactivation, purification, and formulation steps.

The facility where final product filling took place had an automated Environmental Monitoring System (EMS) and Building Management System (BMS) to monitor room pressure differentials, temperature, and relative humidity. Environmental monitoring for viable and non-viable particles was performed during aseptic filling.

The deficiencies identified in this section have been adequately addressed and will be verified during future inspections.

Sanitation and Hygiene

Premises and equipment in the production areas were maintained at a satisfactory level of cleanliness at the time of inspection. Personal hygiene and sanitation appeared satisfactory. Areas were cleaned in accordance with approved written procedures. Personnel were observed performing their duties in an organized manner.

Qualification and Validation

A validation master plan was in place. The following validation and qualification activities were reviewed:

Aseptic Process Simulation (Media Fill): Media fills were executed using TSB media, with pre- and post-filtration filter integrity testing and growth promotion testing using pharmacopoeial reference cultures.

Interventions on Aseptic Lines: Smoke studies for interventions were executed and documented. Both open-door and closed-door interventions were covered.

Container Closure System Compatibility Studies: Extractables and leachables studies were performed per USP Chapter 1663, for the packaging materials used for storage of antigen bulk. Identified elements were below PDE limits. Leachables studies at the 18-month time point showed all samples below the limit of quantitation.

Seal Integrity Test Method Validation: The vacuum leak test method was validated.

Tunnel Sterilisation/Depyrogenation Qualification: HEPA integrity testing, air velocity, pressure differential, temperature distribution, endotoxin challenge, and particle monitoring were performed.

Transport Validation: Performance qualification of vaccine bulk transportation was conducted, including seasonal verification with identified hottest and coldest points.

The deficiencies identified in this section have been adequately addressed and will be verified during future inspections.

Complaints

Product quality complaints were handled according to a written procedure (SOP BJ-SMP-10-009). Complaints were classified and had defined timelines for investigation and closure. A CAPA would be initiated when required.

The deficiencies identified in this section have been adequately addressed and will be verified during future inspections.

Product Recalls

A procedure for product recalls (SOP BJ-SMP-12-002) was in place. If product quality was affected, a recall would be initiated following this procedure.

Contract Production, Analysis, and Other Activities

No contract production activities were noted for the products within the inspection scope.

Self-Inspection, Quality Audits and Suppliers' Audits and Approval

A procedure for supplier qualification and approval was in place. The annual vendor monitoring quality report was reviewed.

The deficiencies identified in this section have been adequately addressed and will be verified during future inspections.

Personnel

An organization chart was available. Key personnel had appropriate qualifications and experience. The Quality Head (QP) and Production Head were identified, and their responsibilities were defined.

Training

A GMP training programme was in place (SOP BJ-SMP-03-003). Training categories included orientation, continued position training, training upon effectiveness of a document, and specialized training. A 2025 annual master training plan was available.

Personal Hygiene

Personnel hygiene requirements were documented. Gowning procedures were defined for entry to classified areas.

Premises

The manufacturing areas were of a good standard and suitable for the activities conducted. Exposed surfaces were smooth and permitted cleaning.

The HVAC system consisted of 30% fresh air and 70% recirculated air, with primary, secondary, and HEPA filters. The Environmental Management System provided alarms and SMS notifications in case of system failure.

The purified water system included online monitoring of relevant parameters. Provisions for regular sanitization were in place.

The Animal House was inspected, including positive pressure rooms where animals were kept. Tests conducted included abnormal toxicity, pyrogen test, and potency testing.

The deficiencies identified in this section have been adequately addressed and will be verified during future inspections.

Equipment

Production equipment was of good standard and appeared well maintained. Equipment qualification and preventive maintenance were performed. The equipment viewed during the inspection was suitable for the processes allocated.

Materials

Incoming materials were quarantined after receipt until released for use. The receiving checklist included integrity, packaging, COA, temperature conditions for cold chain, and supplier qualification status. Raw materials and finished products were stored under specified conditions.

The deficiencies identified in this section have been adequately addressed and will be verified during future inspections.

Documentation

Documents were designed, prepared, reviewed, and distributed according to approved procedures. Batch manufacturing records for EV71 vaccine bulk and Quadrivalent Influenza Vaccine were reviewed.

Good Practices in Production

Production operations followed clearly defined procedures. During processing, materials, containers, equipment, and rooms were labelled with product name, strength, and batch number. In-process controls were performed. The inspectors toured the production areas including virus purification rooms, vial filling line, and visual inspection station.

The visual inspection for QIV was fully automated with two stations (appearance and content abnormality). The camera detection limit was specified.

The deficiencies identified in this section have been adequately addressed and will be verified during future inspections.

Good Practices in Quality Control

The QC function was independent of other departments. The QC laboratories were appropriately equipped and located separately from production areas. Volumetric solution shelf-life determination studies were performed using a risk-based approach. Stability monitoring was conducted under relevant storage conditions. Appropriate analytical methods were used for testing and these were validated.

The deficiencies identified in this section have been adequately addressed and will be verified during future inspections.

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, **Sinovac Biotech Co. Ltd-Changping, located at No. 15, Zhi Tong Road, Changping Science Park, Changping District Beijing, P. R., China** was considered to be operating at an acceptable level of compliance with WHO cGMP guidelines for the manufacture of Biologics (23-Valent Pneumococcal Polysaccharide Vaccine, Hepatitis A Vaccine, Enterovirus 71 Vaccine and Influenza Vaccine).

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

7.0 References

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