

Prequalification Unit Inspection Services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Finished Product Manufacturer
(VACCINES)

Part 1	General information
Manufacturers details	
Name of manufacturer	Haffkine Bio-Pharmaceutical Corporation Limited (HBPCL)
Corporate and inspected manufacturing site address	Acharya Donde Marg, Parel, Mumbai-400 012, Maharashtra, India.
Inspection details	
Dates of inspection	3 to 6 November 2025
Type of inspection	Routine/Follow-up inspection for: - Bivalent type 1&3 Oral Poliomyelitis vaccine (bOPV) - Monovalent type 1 Oral Poliomyelitis vaccine (mOPV1)
Introduction	
Brief description of the manufacturing activities	Haffkine Bio-Pharmaceutical Corporation Limited (HBPCL) manufactures Oral Polio Vaccines starting from the blending of the sterile polio monovalent bulk received from PT Biofarma (Indonesia). The company is responsible for blending, filling, packaging, labelling, laboratory testing, storage, batch release, and distribution of the bivalent Oral Polio Vaccines (OPV type 1 & type 3) and the monovalent Oral Polio Vaccine (OPV type 1).
General information about the company and site	Haffkine Institute was bifurcated from the Government in 1975, with a view to expanding the production activities to meet the growing demands for medicines and life-saving drugs. The production activities were entrusted to the Haffkine Bio-Pharmaceutical Corporation Limited (HBPCL), a fully owned State Government of Maharashtra Undertaking, registered under the Companies Act, 1956. The Managing Director and the Board of Directors of the Company are appointed by the Government of Maharashtra. HBPCL has expertise in the manufacture and supply of a wide range of Biological and Non-biological products, comprising Bacterial and Viral vaccines, Antisera, Toxoids, injectables, and Pharmaceuticals in the pursuit of its mission of "Service to Mankind in the Health Care Sector. The Company plays a pioneering role in the development and production of a wide range of Bacterial and Viral Vaccines, i.e., diphtheria, tetanus, whooping cough, plague, and poliomyelitis. The company has manufacturing experience in tablets, capsules, oral liquids & external use preparations such as antiseptic creams & antiseptic liquids. HBPCL is located in the centre of Mumbai city, and the total area of the campus is 1,13,286 sq. meters (27.90 Acres). The OPV facility is built in the centre of the available sprawling garden land of HBPCL premises used for the manufacture,

	storage & testing of Oral Poliomyelitis Vaccine only. The facility has independent premises measuring 1778.57 sq. meters.
History	The previous WHO inspection of the site was conducted from 12 to 16 June 2023. The manufacturer has been routinely inspected by the Indian authorities (CDSCO, FDA – Maharashtra, and CDL, Kasauli).
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	OPV Facility and related utilities, warehouses, and QC labs.
Restrictions	None
Out of scope	Products and vaccines other than the Bivalent type 1&3 Oral Poliomyelitis vaccine, IP (bOPV1&3), and the Monovalent type 1 Oral Poliomyelitis vaccine, IP (mOPV1).
WHO products covered by the inspection	FVP-P-200 - Bivalent type 1&3 Oral Poliomyelitis vaccine, IP (bOPV1&3) FVP-P-186 - Monovalent type 1 Oral Poliomyelitis vaccine, IP (mOPV1).
Abbreviations	Meaning
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
APS	Aseptic process simulation
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CCS	Contamination control strategy
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GMP	Good manufacturing practices
GPT	Growth promotion test
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IQ	Installation qualification
LAF	Laminar air flow
LIMS	Laboratory information management system

MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MFT	Media fill Test
MR	Management review
NC	Non conformity
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PUPSIT	Pre-Use Post-Sterilization Integrity Test
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RABS	Restricted Access Barrier System
RCA	Root cause analysis
RO	Reverse osmosis
SIP	Sterilization in place
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer
WFI	Water for injection

Part 2	Summary of the findings and comments
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1. Pharmaceutical quality system

The Pharmaceutical Quality System (PQS) was established through a Quality Manual, effective 1 July 2025. The elements of the pharmaceutical quality system were described within the manual. The document was prepared by Quality Assurance, approved by Production, and authorized by senior management. Responsibilities of senior management, including oversight of quality operations, were defined and assigned to relevant management personnel.

The documentation system was structured into four levels:

1. Quality Manual

2. Procedures
3. Work Instructions and Supplier Manuals
4. Records, including forms, databases, plans, drawings, agreements, contracts, and meeting minutes

A Quality Policy approved by senior management was in place.

The manufacturer had implemented improvements to the PQS following the previous WHO inspection and continued activities to strengthen the maturity and effectiveness of the system. Observations identified during the inspection were satisfactorily addressed through corrective and preventive actions (CAPA) prior to publication of this WHOPIR.

Management Review

A procedure governing management review was in place and specified annual review of the quality system.

Documentation for the most recent management review meeting held in October 2025 was available, including meeting minutes, presentations, and attendance records. Participants included senior management and heads of departments.

Key Performance Indicators (KPIs) had been established to monitor the effectiveness of the quality system. The indicators covered areas including:

- Audits
- Change control
- Complaints
- Deviations
- Document management
- Management review
- Manufacturing facilities
- Utilities and equipment
- Quality agreements

The KPI framework was enhanced following the inspection to improve trending, visualization, and monitoring of additional quality metrics. The related CAPAs were reviewed and considered satisfactory prior to publication of this WHOPIR.

Product Quality Review

Annual Product Quality Reviews (APQRs) were performed in accordance with an approved procedure defining the review cycle, scope, objectives, and approval requirements.

Three APQRs were reviewed during the inspection.

April 2022 – March 2023

During this period, 356 batches of oral poliovirus vaccine were manufactured. All batches complied with established specifications, and no out-of-specification (OOS) or out-of-trend (OOT) results were reported.

The quality management system remained under control, and product quality was considered satisfactory. Six deviations (four major and two minor) and one minor incident were reported and closed. Equipment-related issues and packaging material issues were the most common causes.

One product complaint concerning vial discoloration and breakage was investigated and resolved.

Outstanding actions related to a previous WHO inspection remained in progress due to procurement-related delays and equipment upgrade activities. Vendor development activities for selected raw materials were also ongoing.

April 2023 – March 2024

A total of 177 batches were manufactured. Product quality, safety, and efficacy remained satisfactory, and no OOS or OOT results were reported.

Process capability assessments for critical quality attributes remained satisfactory.

Fifteen deviations were reported, including three critical deviations, all of which had been investigated and closed. Equipment-related issues continued to be the most frequently reported deviation category.

One product complaint related to vial discoloration was investigated and resolved.

The increase in major and critical deviations was evaluated, and actions were taken to strengthen root cause analysis and deviation management processes. Outstanding CAPAs from the previous WHO inspection remained under implementation due to procurement constraints.

April 2024 – March 2025

A total of 59 batches were manufactured, primarily to support national tender requirements and vendor development activities.

Product quality remained satisfactory. No critical deviations, incidents, complaints, recalls, or returns were reported during the review period.

Ten deviations (five major and five minor) were reported. The principal causes were equipment failures, documentation deficiencies, and activities associated with facility and utility upgrades.

Of the CAPAs arising from the previous WHO inspection, the majority had been closed, while a limited number remained open and related to complex procurement and installation activities.

Observations identified during review of the APQR process were subsequently addressed through CAPA and were considered satisfactory before publication of this report.

Quality Risk Management

A Quality Risk Management (QRM) procedure was implemented at the site.

The procedure included the use of recognized risk management tools such as:

- Failure Mode and Effects Analysis (FMEA)
- Fault Tree Analysis (FTA)

- Hazard Analysis and Critical Control Points (HACCP)

The 2025 Risk Assessment Register was reviewed.

A risk assessment related to environmental monitoring was examined. Following the inspection, the approach was updated to strengthen the assessment methodology, justification of risk ratings, and documentation of risk mitigation activities.

A risk assessment for facility disinfection demonstrated identification of medium risks and implementation of actions that reduced risks to acceptable levels.

A risk assessment related to filter integrity verification was also reviewed. Mitigation measures were implemented and demonstrated reduction of the associated risk level.

The observations identified in the quality risk management system were addressed through CAPA to a satisfactory level before publication of this WHOPIR.

Deviation Management

A deviation management procedure was implemented and categorized deviations as minor, major, or critical.

Investigations were required to include root cause analysis, use of a structured investigation methodology, risk assessment, and implementation of corrective and preventive actions where appropriate.

Selected deviation records were reviewed during the inspection.

One deviation concerned a lack of synchronization between computerized monitoring and equipment interface systems. Following investigation and implementation of corrective actions, revalidation activities were completed and the deviation was closed.

A second deviation concerned incorrect identification of microbiological reference strains. Corrective actions were implemented, resulting in successful resolution of the issue, and the deviation was closed.

Opportunities to strengthen root cause analysis and investigation effectiveness were identified during the inspection. These were addressed through CAPA and considered satisfactory before publication of this WHOPIR.

CAPA Management

The manufacturer presented the status of CAPAs arising from the previous WHO inspection.

A major refurbishment project involving replacement and upgrading of the filling and sealing line with a restricted access barrier system (RABS) had been completed. Qualification and validation activities were finalized and the associated CAPA was closed.

At the time of inspection, two CAPAs related to supervisory environmental monitoring and storage temperature monitoring systems remained open due to qualification discrepancies identified during performance qualification. Appropriate remediation plans and completion timelines had been established.

Personnel

The organizational structure demonstrated that Quality Assurance and Quality Control had direct access to senior management on quality matters.

Staffing levels included:

- Quality Assurance: 11 personnel
- Quality Control (Biological): 12 personnel
- Quality Control (Chemical): 10 personnel
- Production: 90 personnel
- Stores: 9 personnel
- Dispatch: 6 personnel
- Engineering: 29 personnel

Personnel were appropriately qualified through relevant education, training, and experience for their assigned responsibilities.

Documentation

The document management system was maintained using a paper-based approach.

Procedures were available governing document preparation, review, approval, revision, implementation, training, and archival.

Opportunities for improvement in document control practices were identified during the inspection and were addressed through CAPA to a satisfactory level before publication of this WHOPIR.

Batch Release Process

Batch release was conducted according to an established procedure.

Quality Assurance reviewed batch manufacturing documentation and production records before further processing and release activities. Following completion of all required quality control testing, results were verified against approved specifications.

Lot documentation and representative samples were submitted to the national control laboratory. Following receipt of compliant results from the national authority, batches were released for distribution.

Distribution activities were conducted under the oversight of the Quality Assurance department.

Lot Summary Protocol

Lot summary protocols were prepared according to an approved procedure.

The protocols reviewed during the inspection contained the relevant manufacturing and quality control information, and batch release decisions were adequately supported by the documented data.

2. Production System

The manufacture of Oral Polio Vaccine (OPV), including preparation of formulation solution, blending of vaccine bulks, sterile filtration, filling, stoppering, sealing, visual inspection, labelling, packaging, storage, testing, and dispatch, was performed within the dedicated OPV facility. No contract manufacturing or contract quality control activities were used for the manufacture, testing, or release of OPV.

Manufacturing activities involving formulation solution preparation, blending, filling, visual inspection, labelling, and packaging were observed during the inspection.

The formulation solution was prepared in a controlled environment using sterilized equipment and filtered through pre-filters and a sterilizing-grade filter prior to use in vaccine formulation. Raw materials were prepared, dispensed, and stored under defined conditions before use.

Blending was performed in a unidirectional airflow workstation located within a controlled cleanroom environment. Vaccine bulks were transferred to a blending vessel containing the required quantity of sterile formulation solution. The formulated vaccine was subsequently transferred to the filling area and mixed according to the validated process.

Restricted Access Barrier System (RABS) gloves were routinely sterilized, integrity tested at defined intervals, and disinfected between manufacturing campaigns. Sporidical disinfection of critical surfaces was performed after each batch, and periodic fumigation of the facility was conducted according to established procedures.

The filling machine was equipped with multiple filling heads. Components in direct contact with the product were sterilized prior to use. In-process controls included routine volume checks performed at predefined intervals throughout filling operations.

Sterile filtration was performed immediately prior to filling using pre-filters and a sterilizing-grade final filter. Filter integrity testing was conducted before sterilization and after use. A risk assessment supporting the filter strategy was available. Samples were collected before filtration for quality control testing, including sterility and physicochemical parameters.

Reusable product-contact tubing and other process components were managed through a controlled lifecycle approach, with maximum use limits established and supported through validation studies and aseptic process simulations.

Cleanroom garments were subject to defined sterilization and reuse limits based on qualification data.

Visual inspection of filled vials was performed using a semi-automated inspection process. Vials were inspected against contrasting backgrounds to facilitate detection of visible defects. Personnel performing visual inspection were qualified and requalified at defined intervals. Illumination levels used during inspection were routinely verified.

Critical defects included container damage and the presence of foreign particulate matter. Defect classification criteria were established and implemented within the inspection process.

Opportunities for improvement related to sampling representativeness and acceptance quality limit (AQL) criteria were identified during the inspection. These observations were subsequently addressed through CAPA and considered satisfactory before publication of this WHOPIR.

Batch Numbering

A structured batch numbering system was used to uniquely identify each finished product batch. The coding system incorporated information relating to product type, vaccine category, year and month of manufacture, and a unique sequential batch number.

Process Validation

Following installation and upgrading of the formulation and filling line, the manufacturing process was revalidated.

Validation batches were manufactured at commercial scale in accordance with an approved validation protocol. The batches underwent testing for critical quality attributes, including potency, formulation composition, pH, and sterility. Stability studies were ongoing at the time of inspection.

The formulation solution used during validation was also tested to confirm consistency with predefined formulation requirements.

Additional validation batches were planned to provide further process performance data.

Based on the results reviewed and compliance with the approved protocol, the manufacturing process was considered validated and demonstrated a satisfactory level of robustness and reproducibility under the upgraded operating conditions.

Observations identified during review of the validation programme were addressed through CAPA to a satisfactory level before publication of this report.

Aseptic Process Simulations

Aseptic Process Simulations (APS), also referred to as media fills, were conducted initially in three consecutive runs and subsequently performed twice yearly.

The most recent media fill programme performed after installation of the upgraded manufacturing line was reviewed during the inspection. The simulation included representative aseptic processing operations and evaluated critical process parameters.

The APS programme incorporated consideration of worst-case conditions, including equipment hold times, sterile component hold times, personnel interventions, and re-use of selected sterilized components. No contamination was detected during the simulation runs.

Growth promotion testing of the culture media was performed using appropriate reference microorganisms and environmental monitoring isolates.

The aseptic process simulation programme demonstrated the capability of the process to maintain aseptic conditions during routine manufacturing operations.

Batch Manufacturing Record Review

Batch manufacturing records reviewed during the inspection included a batch that was under manufacture at the time of inspection.

The records contained the required manufacturing and in-process control data, and production activities were documented in accordance with established procedures. Batch documentation reviewed during the inspection was generally complete and supported traceability of manufacturing operations.

Any observations identified during review of batch documentation were addressed through CAPA to a satisfactory level before publication of this report.

3. Facilities and Equipment System

The OPV facility was dedicated to the manufacture and control of Oral Polio Vaccine (OPV). The site manufactured bivalent oral poliovirus vaccine (Types 1 and 3) and monovalent oral poliovirus vaccine (Type 1).

The facility included the following areas:

- Raw material storage
- Primary and secondary packaging material storage
- Production areas
- Quality control laboratories
- Finished product storage facilities
- Packaging and dispatch areas
- Engineering and maintenance support services

Chemical quality control activities were performed in a separate quality control laboratory shared with other manufacturing operations.

A major refurbishment of the production area was completed prior to the inspection. The project included replacement and upgrading of the washing, depyrogenation, filling, and sealing equipment and installation of a Restricted Access Barrier System (RABS). Qualification and validation activities for the upgraded facility and equipment were completed before routine operation.

Facility layouts, room classifications, personnel and material flows, and pressure cascade schemes were reviewed during the inspection and were found to support appropriate contamination control principles.

The manufacturer had implemented computerized supervisory monitoring systems for critical environmental parameters, including differential pressure and temperature monitoring of storage areas. During qualification activities, performance-related observations such as data variability and intermittent losses were identified. Corrective actions, additional monitoring, and requalification activities were implemented. These observations were subsequently addressed through CAPA and were considered satisfactory prior to publication of this WHOPIR.

Qualification and Validation

A Validation Master Plan (VMP) was in place and described the qualification and validation strategy for facilities, utilities, equipment, and supporting systems.

Qualification activities included, as appropriate:

- User Requirement Specifications (URS)
- Design Qualification (DQ)
- Factory Acceptance Testing (FAT)
- Installation Qualification (IQ)
- Operational Qualification (OQ)
- Performance Qualification (PQ)
- Periodic Requalification

An annual qualification and validation programme was established and maintained.

Key qualification activities included:

- HVAC Systems: The heating, ventilation, and air conditioning (HVAC) systems were routinely requalified.
- Water Systems: Water systems were qualified using a phased approach that included intensive monitoring during initial qualification followed by routine monitoring under normal operating conditions.
- Pure Steam System: the pure steam system was routinely qualified and monitored through testing of critical steam quality attributes, including: Non-condensable gases, Dryness fraction, Superheat. Condensate quality was verified against pharmacopoeial requirements for Water for Injection (WFI).
- Compressed Air System: Compressed air systems used in manufacturing operations were subject to periodic qualification and monitoring.
- Sterilization Equipment: autoclaves and depyrogenation equipment were routinely qualified to verify continued compliance with validated operating parameters.
- Cold Chain Storage: Cold rooms and deep freezers used for storage of vaccines and critical materials were periodically qualified to demonstrate maintenance of specified temperature ranges.
- Aseptic Process Simulations: APS was performed at defined intervals as part of the ongoing process verification programme.

Opportunities for improvement identified during qualification and validation activities were addressed through CAPA and considered satisfactory before publication of this WHOPIR.

Water and Pure Steam Systems

Purified Water (PW) was produced through a treatment system incorporating reverse osmosis and electrodeionization technologies.

Purified water was used for:

Haffkine Bio-Pharmaceutical Corporation Limited, Mumbai, India

3-6 November 2025

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- Feed water to the Water for Injection (WFI) system
- Feed water to the pure steam generator
- Initial washing of primary containers

Water for Injection was generated by a distillation system and stored in a dedicated stainless-steel storage vessel. Distribution was performed through a continuously circulating loop equipped with online monitoring of critical quality attributes, including conductivity and total organic carbon (TOC).

The WFI storage and distribution system was routinely sanitized using pure steam.

A performance qualification programme for the purified water and WFI systems had recently been completed and was being followed by an extended routine monitoring phase. Qualification results reviewed during the inspection complied with established acceptance criteria.

The pure steam system was subject to periodic requalification, including steam quality testing and condensate evaluation. Records reviewed during the inspection demonstrated compliance with predefined specifications.

HVAC

The HVAC system serving the OPV facility underwent periodic performance requalification.

The qualification programme included assessment of:

- Differential pressure cascades
- Air velocity
- Air changes per hour
- HEPA filter integrity
- Recovery performance
- Viable environmental monitoring
- Non-viable particle monitoring

Qualification results reviewed during the inspection demonstrated compliance with predefined acceptance criteria.

Airflow visualization studies were conducted periodically to confirm protection of critical operations and maintenance of appropriate airflow patterns.

Critical processing equipment such as laminar airflow units and transfer systems were also periodically requalified. Testing included airflow verification, particle monitoring, microbiological monitoring, and HEPA filter integrity testing.

Observations identified during review of HVAC qualification documentation were addressed through CAPA and considered satisfactory before publication of this WHOPIR.

Filling and Sealing Equipment

Performance qualification of the vial filling and sealing equipment was performed following installation of the upgraded production line.

The qualification programme challenged the equipment at multiple operating speeds representative of routine manufacturing conditions. Key parameters evaluated included:

- Fill volume accuracy and precision
- Container closure performance
- Equipment operational consistency
- Leak testing performance

The qualification programme concluded that the filling and sealing equipment was suitable for its intended use within validated operating parameters.

During review of qualification documentation, opportunities for improvement in data presentation and recording practices were identified. Appropriate corrective actions were implemented and verified. These observations were satisfactorily addressed through CAPA before publication of this WHOPIR.

4. Laboratory Control System

The Quality Control Department was composed of two sections:

- Biological Quality Control
- Chemical Quality Control

The Biological Quality Control laboratory was located within the OPV facility and was dedicated to microbiological and biological testing, including in-process controls and finished product testing.

The Chemical Quality Control laboratory was located in a separate facility and was responsible for chemical testing of utilities, raw materials, packaging materials, and finished products.

Samples originating from manufacturing operations were transferred to the appropriate testing laboratories through defined sample handling processes.

The inspection identified opportunities to strengthen sample receipt, traceability, and documentation practices. Corrective and preventive actions (CAPA) were subsequently implemented and reviewed to a satisfactory level prior to publication of this report.

The Biological Quality Control laboratory included dedicated areas for:

- Sterility testing
- Potency testing
- Microbiological testing

Reference standards supplied by the national control laboratory were stored under controlled conditions and continuously monitored.

Environmental monitoring media were incubated under predefined conditions, and growth promotion testing was routinely performed using appropriate reference microorganisms and environmental isolates.

Sterility testing was performed using membrane filtration techniques with inoculation into two suitable culture media, in accordance with established procedures.

Reference microorganisms were maintained according to predefined procedures governing storage, propagation, and maximum passage levels.

An automated microbial identification system was available and was used to identify critical isolates recovered from environmental monitoring and utility monitoring programmes. Following inspection observations related to documentation and investigation practices, improvements were implemented through CAPA and were considered satisfactory before publication of this report.

Stability samples and retention samples were stored under qualified temperature-controlled conditions.

The inspection identified opportunities to strengthen stability programme documentation and alignment of release and shelf-life specifications. The manufacturer undertook appropriate corrective actions, including revision of relevant procedures and enhancement of stability programme requirements. These actions were reviewed and considered satisfactory before publication of this report.

The in-use stability programme supporting multidose use of the vaccine was also reviewed. Additional studies were initiated to further support labelled storage and use conditions under conditions representative of field use.

Out-of-Specification (OOS) Management

Procedures governing the management, investigation, documentation, and closure of Out-of-Specification (OOS) results were established for both the Biological and Chemical Quality Control laboratories.

The OOS programme included requirements for:

- Initial laboratory investigation
- Extension of investigation where applicable
- Root cause determination
- Impact assessment
- Corrective and preventive actions

OOS records were reviewed during the inspection.

The manufacturer reported a very low incidence of OOS results. During the inspection, opportunities were identified to further strengthen awareness, identification, documentation, and investigation of potential OOS events to ensure consistency with regulatory expectations and internal procedures.

Corrective actions included reinforcement of OOS procedures, personnel training, and review of historical laboratory data. These actions were assessed and considered satisfactory prior to publication of this WHOPIR.

Environmental Monitoring Results

Environmental monitoring of classified manufacturing areas was performed using a comprehensive monitoring programme that included:

- Settle plates
- Active air sampling
- Surface monitoring
- Personnel monitoring

Monitoring was conducted in accordance with approved procedures and covered both at-rest and operational conditions, as appropriate.

Environmental monitoring data were routinely reviewed and trended. Monthly trend reports were prepared, and annual trend evaluations were incorporated into the Annual Product Quality Review (APQR) programme.

The data reviewed during the inspection demonstrated ongoing monitoring of environmental conditions to support aseptic manufacturing operations.

Any observations identified during review of the environmental monitoring programme were addressed through CAPA and considered satisfactory before publication of this WHOPIR.

5. Materials Management

The raw material and packaging material warehouse was located within the OPV facility. Dedicated storage areas were available for materials according to their status.

Sampling activities were performed in a controlled environment equipped with unidirectional airflow protection. Sampling procedures included identification testing of excipients used in vaccine formulation, and sampled containers were appropriately identified to maintain traceability.

Vaccine bulks were stored in dedicated ultra-low temperature freezers within the production area. Retained bulk samples were stored under the same controlled conditions.

Certain packaging components and shipping materials were stored in a separate storage facility.

Finished products were stored in qualified freezer facilities maintained within the approved temperature range for vaccine storage.

An approved supplier programme was implemented and maintained. Raw materials were subject to appropriate cleaning procedures prior to transfer into storage areas.

The warehouse management system was primarily paper-based and incorporated visual status identification to distinguish materials undergoing testing, approved materials, and rejected materials.

During the inspection, opportunities for improvement were identified in relation to warehouse controls, material status management, and documentation practices. Appropriate corrective and preventive actions (CAPA) were implemented by the manufacturer. These actions were reviewed and considered satisfactory prior to publication of this WHOPIR.

International Shipping

Packaging and dispatch activities were conducted within a designated dispatch area equipped for preparation of international vaccine shipments.

Finished product was packaged in insulated shipping containers qualified for the intended transport conditions. Shipping configurations were designed to maintain the required storage temperature throughout transportation.

Each shipment incorporated temperature-monitoring devices to provide evidence of temperature maintenance during transit.

The packaging and shipping process was performed according to approved procedures and supported by qualified packaging configurations.

Observations identified during review of the shipping and distribution system were addressed through CAPA and considered satisfactory before publication of this WHOPIR.

6. Packaging and Labelling System

Labelling and packaging were performed in a dedicated packaging room.

Vaccine Vial Monitor (VVM) labels were printed online and included batch-specific information such as batch number and expiry date. Labelled vials were manually packaged into cartons containing 50 vials. A package insert was included in each carton, and batch details were printed on a label affixed to the carton. Cartons were labelled and sealed before transfer to cold storage, pending tertiary packaging and shipment.

Labelling and packaging activities for a batch were performed on the same day as visual inspection. The manufacturer did not store unlabelled vials. A maximum holding time outside refrigerated conditions was defined.

VVM labels were stored under frozen conditions. The optical density of each VVM label consignment was checked before use.

The manufacturer operated two labelling machines.

Some deficiencies were noted during the labelling and packaging activities. The corresponding CAPA was considered satisfactory before publication of this WHOPIR.

Part 3	Conclusion – Inspection outcome
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Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, **Haffkine Bio-Pharmaceutical Corporation Limited (HBPCL)**, located at **Acharya Donde Marg, Parel, Mumbai - 400 012, Maharashtra, India** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines.

All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the WHOPIR, were addressed by the manufacturer, to a satisfactory level, prior to the publication of the WHOPIR

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

Part 4	List of WHO Guidelines referenced in the inspection report
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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. **Short name: WHO TRS No. 986, Annex 2**
<https://www.who.int/publications/m/item/trs986-annex2>
2. WHO good manufacturing practices for biological products. WHO Expert Committee on Biological Standardization. Sixty-sixth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 999), Annex 2. **Short name: WHO TRS No. 999, Annex 2**
<https://www.who.int/publications/m/item/annex-2-trs-no-999-WHO-gmp-for-biological-products>
3. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4. **Short name: WHO TRS No. 929, Annex 4**
<https://www.who.int/publications/m/item/annex-4-trs-929>
4. Good manufacturing practices: guidelines on validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-third report. Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3. **Short name: WHO TRS No. 1019, Annex 3**
<https://www.who.int/publications/m/item/trs1019-annex3>
5. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-First Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. **Short name: WHO TRS No. 943, Annex 3**
[http://whqlibdoc.who.int/trs/WHO TRS 943 eng.pdf?ua=1](http://whqlibdoc.who.int/trs/WHO_TRS_943_eng.pdf?ua=1)
6. WHO good practices for pharmaceutical quality control laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-seventh report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052, Annex 1. **Short name: WHO TRS No. 1052, Annex 4**
<https://www.who.int/publications/m/item/who-good-practices-for-pharmaceutical-quality-control-laboratories>
7. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3. **Short name: WHO TRS No. 957, Annex 3**
<https://www.who.int/publications/m/item/trs957-annex3>

8. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-sixth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 2. **Short name: WHO TRS No. 1044, Annex 2**
<https://www.who.int/publications/m/item/trs1044-annex2>
9. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7. **Short name: WHO TRS No. 961, Annex 7**
https://extranet.who.int/prequal/sites/default/files/document_files/TRS_961_Annex7_2011.pdf
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