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

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**Zydus Lifesciences Limited**
Corporate address of manufacturer	Zydus Corporate Park Scheme No. 63, Survey No. 536, Khoraj (Gandhinagar), Nr. Vaishnodevi Circle, S G Highway, Ahmedabad- 382 481, State - Gujarat, India.
Inspected site	
Name & address of inspected manufacturing site if different from that given above	1. Plot Survey No. 23, 25/P, 37, 40/P, 42 to 47, 49 & 50 Sarkhej- Bavla N.H. No. 8A, Opp. Ramdev Masala, Village - Changodar, Tal: Sanand Dist.- Ahmedabad- 382 213, State – Gujarat, India 2. Survey No.: 417, 419 and 420, Sarkhej-Bavla, N. H. No. 8A, Moraiya, Tal: Sanand, Dist. Ahmedabad -382 210. State - Gujarat, India.
Inspection details	
Dates of inspection	3-7 June 2024
Type of inspection	Initial inspection for ZyVac® TCV - Typhoid Vi Conjugate Vaccine and Routine inspection for VaxiRab N - Rabies Vaccine, Human
Introduction	
Brief description of the manufacturing activities	Zydus Lifesciences Limited (formerly Cadila Healthcare Limited) was established in 1951 in Ahmedabad. Zydus Lifesciences Limited is a fully integrated, global healthcare provider, with strengths all along the pharmaceutical value chain. With a core competence in the field of healthcare, Zydus Lifesciences Limited provides total healthcare solutions ranging from vaccines, biologicals, formulations, active pharmaceutical ingredients, animal healthcare products, and wellness products. In 1995, following a restructuring, Zydus Lifesciences Limited commenced operations. Zydus Lifesciences products are exported to over 40 countries. Zydus Lifesciences Limited has diversified into bulk drugs, pharmaceuticals, vaccines, food products, veterinary products and pharmaceutical machine manufacturing.
General information about	The Changodar site of Zydus Lifesciences Limited, has an open plot area of 26.40 acres (1,06,840 m^2) of which 812.5 m^2 area is covered by Vaccine

the company and site	Technology Centre, 2487.23 m^2 area is covered by Bacterial Vaccines Plant, 2006.5 m^2 area is covered by Live Viral Vaccine Production Plant, 2082.55 m^2 area is covered by Inactivated Viral Vaccine Plant, 601.76 m^2 area is covered by Fill-finish Vaccine plant, 199.64 m^2 area is covered by Recombinant Vaccines Production plant, 96.81 m^2 area is covered by Cell and Seed bank storage facility, 1382 m^2 is covered by Quality Control Lab-2, 2205m^2 area is covered by Viral Vaccine facility Plant-, 2178m^2 area is covered by Fill finish vaccine-2, 1988 m^2 area is covered by Central Packaging Facility and 4284m^2 area is covered by central warehouse facility. The production complex of Zydus Lifesciences Limited at the Changodar site also houses Zydus Biologics Division, which manufactures bio-similar products, and is situated in different buildings totally separate from the Vaccine Technology Centre. The formulations plant located at Moraiya Ahmedabad is spread over 40 acres with a built-up area of 1,01,771 m^2. The plant also manufactures tablets, capsules (hard & soft gelatin), aerosols, nasal spray, transdermal patches, liquids and Lyophilized Injectable small volume parenteral.
History	The last WHO PQT inspection for the VaxiRab N - Rabies Vaccine manufacturing site (Moraiya) was conducted from 20 to 24 November 2017.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Changodar site - Vaccine Technology Centre (VTC): • Plant-3A - Bacterial Vaccines Plant - Manufacturing of concentrated bulk of Typhoid Polysaccharide • Plant-2 - Manufacturing of Tetanus Toxoid bulk • Plant-3B/SVP 1 - Fill Finish of Bacterial Vaccines • Plant-10 - Cell and Seed bank storage facility • Plant-11 - Quality Control Lab • Plant-14A - Central Packaging Facility • Plant-14-B - Central warehouse Facility • Related utilities areas Moraiya site: • Inactivated viral vaccine (DS1) facility – Rabies DS manufacturing • Vaccine R Facility – Fill and Finish of Rabies vaccine • Related Quality Control Laboratories, Utilities and Warehouse
Restrictions	During the inspection, there was no production of the Tetanus Toxoid.
Out of scope	Products and vaccines not submitted for prequalification were out of the scope of this inspection.
WHO products covered by the inspection	• ZyVac® TCV - Typhoid Vi Conjugate Vaccine, Multi-dose vial (5 doses, 2.5ml) • VaxiRab N (Rabies vaccine, human) – Single dose vial (Lyophilized)
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APQR	Annual product quality review
APS	Aseptic process simulation

BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
GMP	Good manufacturing practices
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
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
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
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 (where applicable)

1. Pharmaceutical quality system

Zydus Lifesciences Limited had a defined quality system in place. The firm's commitment to quality was stated in the Quality Policy. The QMS system was designed based on ICH Q9, Q10, Schedule M and applicable WHO TRS guidelines.

The Quality Manual stated the Quality Policy and defined the QMS. The quality unit was coordinated for the effective implementation and execution of quality attributes in a systematic and approved manner that aligned with regulatory and cGMP requirements. The independent quality unit consisted of Quality Assurance (QA) and Quality Control (QC). Senior management was responsible for establishing and maintaining the established quality system. All employees were responsible for complying with quality regulations as implemented by the quality department.

Management review (MR):

The central quality unit conducted management-level meetings in accordance with quality policy. The topics for discussion included but were not limited to the status of the actions of the previous meeting, number of critical events, batch failures, recall, stability failures, complaints, confirmed/unconfirmed OOS, audit observations (internal, external, regulatory), overdue CAPA, repetitive deviations, training status, overdue calibration, and PM, APQR, the status of re-validation and re-qualification activities.

Once every four months a Management Technical Review Meeting was conducted in the presence of site heads. The quality parameters discussed included but were not limited to quality initiatives and achievements, quality and facility improvement plans, internal/external audits, overdue regulatory commitments, lot acceptance rates, OOS, recall, complaints, etc. The last meeting minutes were presented.

A monthly meeting was conducted at the site level. Topics discussed included but were not limited to number and rate of overdue CAPA, number of critical events, complaints received, number of repetitive complaints, recalls, lot acceptance rate, OOS, OOT, training status, overdue calibration and PM, APQR, status of re-validation and re-qualification activities, stability summary review. KPIs were defined. Minutes of the last meetings were presented, with the attendance record of the senior management of the site.

Product quality review:

Procedures for preparing, reviewing, and approving the Annual Product Quality Reviews (APQR) to evaluate the process, performance, and quality of all products produced were in place. APQRs were prepared for every calendar year. The outcome was discussed in the Quality Review Meeting (held every month). The APQRs for Rabies and Typhoid conjugated vaccines were spot-checked during the inspection.

Quality risk management:

The company had in place a policy for Quality Risk management already aligned with ICH Q9(R1). Risk assessments were carried out to establish documented evidence of the suitability of the facilities, reliability, and consistency of the equipment, and validity of the manufacturing processes for the intended purpose with no risk or acceptable risk limits. Different tools were used for QRM.

Some QRM reports were spot-checked during the inspection.

Contamination Control Strategy (CCS)

A procedure was in place for the preparation of the Contamination Control Strategy (CCS). Initially, a qualitative Preliminary Hazard Analysis (PHA) was prepared for each vaccine. Then, a quantitative risk assessment (FMEA) with RPN calculation was obtained, and a risk management report was prepared to identify the risks and define CAPAs. The CCS was planned to be reviewed at a minimum of once every two years. The CCS for the vaccines under the scope of the inspection was reviewed.

Deviation management:

A software-based system was implemented to handle deviations, CAPA, change control, Lab incidents, market complaints, and OOS/OOT management. The deviation treatment workflow was managed in accordance with a written procedure. The risk-based deviation categories typically included minor deviations, major deviations, and critical deviations. All these types of events were first addressed by corrections (as applicable) and root-cause investigations. The deviation management process flow typically followed the steps: identification, reporting, investigation, documentation, implementation, monitoring, follow-up, and closure. Deviation-related documents were linked together to promote information traceability.

Some deviations were spot-checked in the system, including reporting, investigation, review, approval, CAPA implementation and its effectiveness and closure.

CAPA management:

Handling of CAPA (Corrective action and preventive action) was through a software application as per specific SOP. CAPA were initiated as an outcome of an investigation or root cause analysis/inspection observation.

Change control (CC):

The change management system was handled according to a written procedure in an electronic system. Changes in the approved facility, equipment, material, process, formula, analytical and/or controls were routed through the change control system. Change control was initiated and reviewed by trained representatives from appropriate disciplines, including quality, regulatory and other concerned departmental persons. Changes were handled as per the respective SOP of the respective site and implemented only after the approval by QA. Changes were categorized as critical, major and minor. The list of change controls for the vaccines under the scope of the inspection for 2024 was presented, and some changes were spot-checked.

Complaints:

Market complaints were handled as per a written SOP. Complaints were logged in an electronic system and investigated by an investigation team in order to find out the probable root cause as per the respective SOP, and decisions were made for the batch disposition. Complaint categorization was done as critical, major, minor and non-substantiated complaints in consultation with production heads. The QA Head evaluated the adequacy of information received along with the complaint, and if any additional information was needed, the QA Head attempted to collect the required information and documented it in the investigation report.

Timelines for preparing the investigation report of a received market complaint and identifying the root cause, followed by the closure of the investigation after initiating necessary corrective and preventive actions, were defined. The final investigation outcome was submitted to the Central Market Complaint cell for further submission to the complainant as a response.

Trending of complaints was performed on a quarterly and yearly basis. No complaint was received in 2024 for the products under the scope of this inspection. The trending report for 2023 was spot-checked. ***Product recalls:***

Product recall activities were handled as per the respective SOP. Product recall can be initiated for customer complaints found to be critical/major, detection of major cGMP failure, and failure result of ongoing stability testing and upon confirmation of serious adverse drug reaction. Recall can be voluntary or statutory. The product recall was classified as classes 1, 2, and 3 depending upon the type of defect, and recall action shall be initiated within defined timelines in SOP, which may include notification of customers and competent authorities, and segregation of recalled products. Mock recall was performed every 2 years in case of no real recall was performed.

A product mock recall protocol was presented. Reconciliation of the product could be achieved.

Self-inspection:

Self-inspection (internal audit) was performed as per respective procedure. A self-inspection system, coordinated by the site compliance cell and executed by independent qualified auditors was designed and conducted to monitor the implementation of and compliance with Good Manufacturing Practice and Good Distribution Practice principles and to propose and monitor necessary corrective measures. The self-inspection system (unannounced or announced) consisted of internal system and/or process/product/system audits based on the checklist and walk-through audits.

On an annual basis, a self-inspection schedule was prepared and approved. The audits were performed as per the schedule.

Quality audits and suppliers' audits and approval:

The raw materials and critical components used in the manufacturing of the vaccines at Zydus were selected and evaluated in accordance with the appropriate/acceptable quality standards. The Zydus Lifesciences site had a process in place to identify, qualify, approve, and maintain the material and service suppliers used in the support of GMP and GDP activities as described in relevant SOPs.

The approved vendor list for API/excipient/packing material was presented.

Contract production, analysis and other activities and Quality agreements:

GMP compliance for the contract laboratories was assessed according to the respective procedure. Outsourced activities like analytical testing, maintenance, calibration, and validation of various support systems were being done through approved technical assistance centers/ laboratories, and other GMP services were performed by the site as per SOP. Quality Agreements were signed to ensure that the quality of materials or services outsourced by a contract organization fulfilled cGMP requirements. Contract organizations were subject to periodic audits by the Zydus GMP supplier qualification group to assess the facility's GMP compliance status. An updated list of contract manufacturers and contract laboratories was provided.

Personnel

Organization, organogram, independence of production from quality control:

The organization chart was provided in the opening meeting as the current version of the SMF. The site organogram and key personnel information were also provided. Quality operations were independent of the production department.

Many employees had a bachelor's or master's degree or above. The interviewees showed good expertise and knowledge concerning vaccine production and related activities during the plant walk-through. The departments at the sites, including manufacturing and development, Quality control, engineering, and quality assurance, appeared to have a sufficient number of personnel with appropriate qualifications with respect to education, experience, and training to perform the desired functions.

- ***Training:***

As per Training SOP, the training management has been driven by an electronic system. Typically, the types of training offered to all employees included new hire (induction) training, on-the-job training, annual GMP training, specific subject training, and retraining if required.

Personnel engaged in GMP activities were qualified to perform their assigned function or duty as established by their job requirements. Personnel may only become qualified to perform a function or duty through education, experience, training, or a combination thereof.

Overall, the personnel were qualified and trained according to the requirements of their positions, and a continuous training program was in place. All staff members participating in the GMP manufacturing activities were properly trained before starting work, and some record-keeping was available and spot-checked.

Details of employee-specific qualifications were available upon request from the training department. Some records were spot-checked.

- ***Personal hygiene:***

The hygiene requirements for the Zydus site included strict adherence to proper hand washing and disinfection techniques and restriction of smoking, eating, drinking, and chewing. Approved entry and exit procedures for the manufacturing workshops, displaying photographs or pictograms as reminders.

The manufacturing workshops had dedicated airlocks for personnel and material, based on different cleanliness levels. Personnel wore specialized clothing to prevent the spread of particles and microbiological agents, serving as a protective barrier.

Employees received regular training on gowning and entry/exit procedures and underwent regular medical check-ups. When entering a restricted area, employees changed from their regular clothes to manufacturing gowning following specific site procedures. Additional gowning was necessary when entering Class D, C, and B rooms.

As a rule, all production area employees were healthy and could not enter the manufacturing facilities if they had open wounds. Besides, all employees were oriented to report sickness to their managers. Operators with infectious diseases were not allowed to work in manufacturing products. Monitoring of health conditions and action taken regarding personnel who may introduce microbial contamination in the manufacturing workshops were documented in relevant SOPs.

Visitors also should report sickness or other relevant health conditions to their host.

- ***Qualification of aseptic operators in Grade B areas:***

An aseptic gowning qualification program was established for grade B areas to assess personnel's ability to maintain an acceptable level of hygiene after gowning to minimize contamination of clean area clothing. Clean and sterile protective garments were provided for every worker in grade A/B area during each work shift. Gloves were regularly sanitized during operations, and masks and gloves should be changed at least after every work session. Additionally, sanitized goggles are worn in grade A and B areas.

Key components of a compliant aseptic personnel gowning program included initial training and education, gowning training, practice, observation, qualification to enter grade B areas and program maintenance.

Some operators' job description and gowning qualification records were spot-checked.

- ***Qualification of visual inspectors:***

A visual inspector qualification protocol was established to qualify the visual inspector's ability to identify and categorize defects within the specified quality attributes, thereby establishing a visual qualification procedure for the filled glass vials (see details visual inspection section). The content of this protocol also established the conditions to reproducibly detect and remove units of vaccines with predefined defects in a controlled process, the acceptance criteria, the re-qualification criteria, and the documentation to be used in the qualification of visual inspection.

An updated requalification record for a manual visual inspector and his biannual eye check-up form in the packaging department were reviewed.

Documentation:

As per the Quality Manual, the Quality System was documented at three levels:

- Level I: Quality Policy and Apex Documents (SMF, Quality Manual, Quality Policy, etc.).
- Level II: SOPs, Protocols, Specifications, Methods, Drawings, etc.
- Level III: All templates, logbooks and records.

The documentation systems used at the Zydus site outlined the processes for creating, reviewing, approving, revising, issuing, distributing and reconciling controlled GMP documents. These documents included Standard Operating Procedures, batch records, forms, specifications, logbooks, laboratory notebooks, and many others. They encompassed electronic and manual processes and were detailed in relevant approved procedures. The site SOPs and central quality SOPs/policies were maintained in the electronic document management system.

Several SOPs and records were spot-checked.

Batch Release Process and Lot Summary Protocol:

The Batch manufacturing and packing records were prepared by the user, reviewed by concerned department representatives, and approved by QA. All the production activities and in-process control attributes were recorded in Batch manufacturing records by production/ QA. Finally, after production of a batch, all the BMRs and BPRs were reviewed by QA. All incoming intermediates, drug substances and finished product samples were tested by quality control department/ in-process quality control department and certificate of analysis (COA) was approved by analytical QA, confirming acceptance of the batch as per pharmacopoeia and regulatory requirements. Batches were quarantined, rejected or released by qualified and authorized QA personnel based on a certificate of analysis, ensuring compliance with product specifications. The Lot Summary Protocol (mentioning production parameters and quality control test results at each stage, up to the finished product) of the batch was submitted to the Central Drug Laboratory (CDL), Kasauli, along with samples for analysis and release. After the batch release letter is received from CDL mentioning lot, manufacturing date, expiry date and

doses for release of the vaccine batch, the batch was released by authorized QA personnel for its intended use.

2. Production system

In general, the production operations were performed by trained personnel, as per respective SOPs. Batch Manufacturing Records (BMR), with detailed instructions to perform and record a processing activity, were in place.

The cell/seed bank storage facility at Changodar site was visited. The freezers were cleaned and in a calibrated status. The logbook was found in compliance. At the time of the visit, the freezers met the qualification standards. Seed lots were stored in two controlled separate locations.

Materials were pre-weighed by the warehouse according to production requests. After dispensing, these materials were stored in the day store area and moved to the preparation room on the day of production. The production equipment in the areas visited was clearly marked, and their qualification status were indicated on visible labels. Documentation related to the processes was readily available in the respective processing rooms. In-process control tests were conducted and recorded.

Process Validation

The strategy for process validations was described in the Validation Master Plan in 3 stages:

- Stage 1 – process design
- Stage 2 – process qualification
- Stage 3 – Continued process verification

The process validation, including the sterile filtration, for Typhoid vaccine underwent a review. The parameters and test results were within predefined acceptance criteria.

The process validation protocol for rabies vaccine to support the introduction of sterile filtration was also spot-checked. Critical parameters and critical materials attributes were defined and studied accordingly. Based on the results and quality attributes included in the study, it could be considered that this process is validated for the manufacturing of commercial-scale batches of the rabies vaccine manufactured at Zydus.

Batch manufacturing record review (BMR):

Some of batch records were reviewed during the inspection.

3. Facilities and equipment system:

Vaccine Technology Centre (VTC), Changodar – Typhoid Conjugated Vaccine

The design of the facility was segregated into different sections based on the type of vaccine to be produced, and each section was further divided with respect to activities carried out, like the upstream process and the downstream process. A fill-finish facility associated with bacterial vaccines was equipped with a formulation vessel, vial washing machine, depyrogenation tunnel, vial/PFS filling and stoppering machine, sealing machine. A central packing facility was available, equipped with visual

inspection booth, labeling machine, and packing area. Dedicated HVAC systems and utilities were provided for all the critical activities to avoid cross-contamination. Filling machine was equipped with oRABS and extended LAF was available for RABS door opening.

Layouts and flow charts of the production areas along with warehouse and quality control area showing the room classification, pressure differentials between adjoining areas, and man/material flow were presented.

Moraiya Site – Rabies Vaccine

The Rabies Vaccine production was conducted in the areas denominated Inactivated Viral Vaccine facility and Vaccine R facility.

The Moraiya site DS facility comprised dedicated workshops for manufacturing of final bulk of rabies vaccine with 3 major areas: egg receipt & incubation, infected area/virus processing area and non-infected area (media preparation, virus inactivation and final bulk preparation).

The principles for flow of personnel, material, product, equipment, samples, waste followed a unidirectional flow to avoid cross contamination.

The Vaccine R Facility was used for material/component preparation, vial filling, lyophilization, cap sealing, packaging and dispatch of Rabies Vaccine.

The RABS integrated filling machine was surrounded by Grade B and provided filtered air through terminal supply HEPA filters. The loading and unloading of partial stoppered filled vials into the freeze dryer took place under grade A.

Qualification and validation:

A Validation Master Plan was in place to ensure facilities/equipment were qualified and all systems re-validations/re-qualifications were carried out in defined frequencies, wherever required, to ensure the consistency of facility and equipment. Execution of the qualification/validation activities was carried out by the validation team (consists of representatives from engineering, user and QA) through approved protocols. Results generated during the validation/ qualification activity were reviewed and approved by QA to ensure compliance with pre-determined specifications and acceptance criteria.

Requalification of equipment, utilities, system were carried out periodically. Area qualification was performed every six months for grades A and B and at least once a year for grades C and D. Sterilizers, lyophilizers, pure steam, controlled temperature equipment, vial washing, shakers, and fermenters were requalified once a year. Aseptic Process Simulation for DP was performed every 6 months and once a year for DS.

Several qualification and validation documentation were spot-checked.

4. Laboratory control system

Quality Control (QC) was an independent function, separate from the production and other departments. QC carried out testing of all raw materials, packing materials, intermediate products and final products. Besides that, quality control analyzed critical utilities like purified water, water for injection, pure steam, compressed gases, etc. The QC used a Laboratory Information Management System (LIMS) software for analytical data management.

In general, the quality control unit had adequate facilities, trained personnel, and approved procedures available for sampling, inspecting, and testing finished products.

Samples collected from manufacturing workshops were sent to relevant laboratories for analysis. This ensured that all raw data related to test performance could be traced in LIMS following the sample workflow.

Classified areas of the manufacturing and quality control laboratories were monitored as per respective Environmental Monitoring Program. Alert and action levels were defined. Trends were evaluated in a defined frequency. Microbial identification was performed as per SOP. The trend reports for the manufacturing areas under the scope of this inspection were spot-checked.

The sterility test was conducted in aseptic conditions.

Products at intermediate / final stages were tested against pre-determined approved specifications as per respective testing SOPs by quality control unit. These were released to their subsequent stage or market upon comply with all the parameters. Records were made manually, by recording instruments or directly inserted in the LIMS systems.

Quality Control unit was also responsible for evaluating the stability of the products at different stages.

Animal house:

Animal house-related tests were conducted at the Moraiya site, which had a dedicated animal house used for in-vivo testing of various vaccines. The facility was adequately equipped with housing and management of various small animal species for routine testing activities of vaccines. In-vivo testing facility comprised of a dedicated floor for the breeding of animals and testing of bacterial, viral, and recombinant vaccines. Containment facilities were designed with appropriate change rooms, wet showers, and a dedicated HVAC system.

Out-of-specification (OOS) management:

A procedure was in place for handling out-of-specification (OOS) issues and recorded in an electronic system. This involved conducting and concluding OOS investigations at different stages, interpreting results, managing inconclusive results, retesting and resampling, appropriate use of averaging, and proper application of outlier tests. All investigations, conclusions, decisions, and corrective actions were documented and preserved as part of the official laboratory records for that specific lot.

Some OOS investigation reports were spot-checked.

5 Materials management:

Upon receipt at the central warehouse, purchased materials from qualified suppliers were checked for identity, vendor, and quantity and logged in the ERP system. An in-house batch number was assigned for every incoming batch. From this stage on, the ERP controlled the status of all goods in the warehouse.

Materials were sampled in a designated room under a reverse laminar air flow bench and identified according to sampling instructions. Based on the analysis results, the QC department approved or rejected the raw materials.

Starting materials, packaging materials and finished products were stored on pallets in racks or on shelves in a warehouse or in storage areas with designated storage conditions, if applicable. In the warehouses, temperature was measured, registered and continuously monitored. Pest control program was implemented in all surrounding area.

Printed packaging materials like labels and cartons were stored in a secure area with access restricted authorized personnel.

Rejected material was accordingly labelled/identified and transferred to a dedicated secure location in the warehouse, where it was held pending a decision on means of disposal (e.g., return to supplier, destruction). The damaged or improperly labelled goods identified at the time of receipt are separated and sent for disposal or return.

The final bulk produced from the respective production block was stored at its recommended temperature. The finished product was stored in cold rooms at the recommended temperature.

Released materials were dispensed in the Grade D dispensing area and delivered to manufacturing.

An SOP described the steps of converting the semifinished to finished product for export. The shipping validation was executed.

6 Packaging and labeling system:

The packaging and labeling operations were carried out per relevant procedures. Serialization through the assigning of a predetermined coding to each product, conferring a unique identity allowed the tracking of the product at any moment in time.

Part 3	Conclusion – Inspection outcome

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, **Zydus Lifesciences Limited**, located at **Plot Survey No. 23, 25/P, 37, 40/P, 42 to 47, 49 & 50, Sarkhej- Bavla N.H. No. 8A, Opp. Ramdev Masala, Village - Changodar, Tal: Sanand Dist.- Ahmedabad- 382 213, State – Gujarat, India** and **Survey No.: 417, 419 and 420, Sarkhej-Bavla, N. H. No. 8A, Moraiya, Tal: Sanand, Dist. Ahmedabad -382 210, Gujarat State, 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

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO TRS No. 986, Annex 2***

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***

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***

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***

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***

6. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1.
   Short name: WHO TRS No. 957, Annex 1

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

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***

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***

10. Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9. ***Short name: WHO TRS No. 961, Annex***

11. 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. ***Short name: WHO TRS No. 961, Annex 2***

12. WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14. ***Short name: WHO TRS No. 961, Annex 14***

13. 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. ***Short name: WHO TRS No. 981, Annex 2***

14. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3. ***Short name: WHO TRS No. 981, Annex 3***

15. WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4. ***Short name: WHO TRS No. 992, Annex 4***

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