EDA Public Inspection Report (EDA-PIR) of biological products

Part 1	***General information***
Manufacturers details	
Company information	
Name of manufacturer	*Zydus life sciences limited vaccine technology center*
Inspected site	
Address of inspected manufacturing site	*Plot Survey No. 23, 25/P, 37, 40/P, 42 to 47, 49 & 50* *Sarkhej- Bavla N.H. No. 8A, Opp. Ramdev Masala, Village - Chandar, Tai: Sanand, Dist.- Ahmedabad - 382 213* *Telephone number: +91-2717-664600* *Fax: +91-2717-664600* *Email address: Kapil.Maithal@zyduslife.com*
Inspection details	
Dates of inspection	*From 03 to 07 February 2025*
Type of inspection	*Overseas inspection prior registration of MMR vaccine* ***(drug substance - drug product)***
Introduction	
General information about the company and site	• *Live Viral Vaccine Plant (Plant-4) For manufacturing of drug substance of Live Viral Vaccines (Mump, Measles, Rubella)* • *3 laboratories for handling each of Measles, Mumps, Rubella virus separately. Formulation and filling are carried out in dedicated facility.* • *Fill finish facility (Plant-5/SVP 2) For filling of Live Virus Vaccines*
Brief report of inspection activities undertaken	
Scope and limitations	
Areas inspected	*Live Viral Vaccine Plant (Plant-4) is designed to manufacture and store concentrated bulk (single harvest) of Measles, Mumps, Rubell and varicella virus in dedicated blocks of Live Virus Production section. The facility is segregated based on the process activity such as media preparation, normal cell culture area, virus culture lab (4 laboratories for handling each of Measles, Mumps, Rubella and varicella virus separately.) Formulation and filling are carried out in dedicated facility. Fill finish facility (Plant-5/SVP 2) is equipped with formulation vessel, vial washing machine, Depyrogenation tunnel, vial filling and stoppering machine, Lyophilizer, sealing machine, visual inspection booth, labeling machine and packing hall. Dedicated AHU and utilities are available for all the critical activities to avoid the cross contamination. The facility is approved by FDCA, Gandhinagar.*

	Quality management system, QRM, personnel, qualification, warehouse of raw materials, finished products warehouse, Production system, laboratories, Packaging and labelling system
Restrictions	*None*
Out of scope	*None*
Inspected biological product	*Live Viral Vaccines (Mump, Measles, Rubella)*
Abbreviations	
AHU	*Air Handling Unit*
ALCOA	*Attributable, Legible, Contemporaneous, Original and Accurate*
API	*Active Pharmaceutical Ingredient*
APQR	*Annual Product Quality Review*
BDL	*Below Detection Limit*
BMR	*Batch Manufacturing Record*
BPR	*Batch Packaging Record*
CAPA	*Corrective Actions and Preventive Actions*
CC	*Change Control*
CFU	*Colony-Forming Unit*
CoA	*Certificate of Analysis*
CpK	*Process Capability Index*
CPP	*Critical Process Parameter*
CQA	*Critical Quality Attribute*
DQ	*Design Qualification*
EM	*Environmental Monitoring*
FAT	*Factory Acceptance Test*
FBD	*Fluid Bed Dryer*
FMEA	*Failure Modes and Effects Analysis*
FPP	*Finished Pharmaceutical Product*
FTA	*Fault Tree Analysis*
FTIR	*Fourier Transform Infrared Spectrometer*
GC	*Gas Chromatograph*
GMP	*Good Manufacturing Practice*
HACCP	*Hazard Analysis and Critical Control Points*
HPLC	*High-Performance Liquid Chromatograph*
HVAC	*Heating, Ventilation and Air Conditioning*
IR	*Infrared Spectrophotometer*
IQ	*Installation Qualification*
KF	*Karl Fisher*
LAF	*Laminar Air Flow*
LIMS	*Laboratory Information Management System*
LoD	*Limit of Detection*
LOD	*Loss on Drying*
MB	*Microbiology*
MBL	*Microbiology Laboratory*
	Master Formulae

MF	*Management Review*
MR	*Nuclear Magnetic Resonance Spectroscopy*
NMR	*National Regulatory Agency*
NRA	*Operational Qualification*
OQ	*Process Hazard Analysis*
PHA	*Preventive Maintenance*
PM	*Process Performance Index*
PpK	*Performance Qualification*
PQ	*Product Quality Review*
PQR	*Pharmaceutical Quality System*
PQS	*Quality Assurance*
QA	*Quality Control*
QC	*Quality Control Laboratory*
QCL	*Quality Risk Management*
QRM	*Risk Assessment*
RA	*Root Cause Analysis*
RCA	*Standard Operating Procedure*
SOP	*Total Aerobic Microbial Count*
TAMC	*Total Fungi Count*
TFC	*Thin Layer Chromatography*
TLC	*User Requirements Specifications*
URS	*Ultraviolet-Visible Spectrophotometer*
UV	

Part 2	***Brief summary of the findings and comments***

1. Pharmaceutical Quality System

1.1 Management review

SOP for management review was reviewed, and it was found 3 management review teams (STRM-CTRM-MTRM). In addition, examples on implementation of these management reviews are Meeting for management review site technical review meeting (STRM) was held based on SOP on 26/11/2024, and Meeting for management review corporate technical review meeting (CTRM) on 10/2024.

1.2 Product quality review

The Annual Product Quality Review (APQR) are prepared for all commercial products which are under manufacturing stage and are marketed as per respective QA SOP of APQR preparation:

- *The APQR are prepared yearly as per the stipulated timeline mentioned in the SOP and include data for all batches manufactured during the said tenure for commercial products only.*
- *The APQR include (but not limited to):*

o Data regarding critical parameters like yield, rejections, and quality control parameters, mean, SRD value. The average, standard deviation, maximum and minimum shall be determined.

o Summary of Change controls carried out during the year applicable for the product.

o Details of Deviations related to the product carried out during the year.

o Details of Batch failure (if any)

o Market complaints (if any)

o Market Authorization

- *Product recall (if any)*
- *Details of Returned goods (if any)*
- *The details of the batches charged to stability and summary of stability data*
- *Details of Out of Specification (OOS) results.*
- *Date of last qualification done, status for equipment/utility qualification and evaluation of batches*

1.3 Quality risk management

- *Zydus lifesciences limited has a well-defined procedure for Quality Risk management in place to provide a systematic approach including principles and tool for Quality Risk management.*
- *Risk assessment is 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 intended purpose with no risk or acceptable risk limits.*
- *The QRM is a framework for gathering documentation, by conducting assessments of various processes, equipment' s, utilities, facilities, systems, support areas, etc., necessary to fulfill the requirements of Current Good Manufacturing Practices (cGMP).*
  - *GAP analysis for drug substance from annex 2 TRS 1044 was done on 17/01/2025*
  - *GAP analysis for drug product from annex 2 TRS 1044 was done 23/01/2025*
- *Some deficiencies were raised in this section that have been adequately addressed & will be verified in the upcoming inspections.*

1.4 Deviation management

Handling of deviations is through an electronic system called Track Wise application as per SOP; this encompasses accountability of action taken departing from an established course or accepted standard enlisting procedure for reporting, investigation, review, approval and closure of deviation.

1.5 Control change

- *Change management system is handled in electronic system called TrackWise application. Any changes in the approved facility, equipment, material, process, formula, analytical and/or controls will be routed through an effective change control system. Change control is initiated and reviewed by trained representatives from appropriate disciplines, including quality, regulatory and other concerned departmental persons. All changes are handled as per respective QA SOP of change control procedure and implemented only after the approval by QA.*
- *The change control system will be applicable for all processes , and many of examples of change control ware selected randomally and checked during inspection.*

1.6 Complaints

- *Market Complaints are received by the QA Head/Designee and investigated by Investigation team to find out the probable root cause as per SOP and decisions are made for the batch disposition based on certain SOP.*

1.7 Product recall

- *Product recall activities are handled as per the respective QA SOP in the proper documentation. Product recall shall be initiated for customer complaint found to be critical/major. After investigation and testing of recalled samples it shall be destroyed in presence of QA person. Information regarding product recall should be notified immediately to higher management and product recalled to closed within one-month period.*
- *Mock recall shall be carried out once in a two year for any product dispatched for sale where maximum distributors are involved, to test the effectiveness of the recall arrangements.*

Effectiveness of recall procedure can also be checked by 'evaluation of a real recall'. Thus, if actual recall is performed, there is no need to perform mock recall. Records of such mock recall should be maintained by the QA department.

1.8 Self-inspection and CAPA managment

- *Self-inspection system is a methodical examination/ review of facilities, quality systems, practices and/or documentation to evaluate its appropriateness for desired purpose, verify compliance with respect to laid down procedures and as per COMP requirements. Self-inspection frequency can be increased for repeated market complaints, rejections, and Quality System failures. A checklist is used for reference, and non-conformance reports are prepared. The head of each department receives the audit report for corrective action. The responsible QA person updates the action plan and verifies compliance status Based on this concept, each unit of Vaccine Technology Centre having an influence on quality, safety and efficacy is subject to periodic self-inspection. Hence the self-inspection for each functional unit by Site internal audit team is performed as per respective SOP.*

1.9 Quality aduits and supplier's audit and approval

The process of approving suppliers was covered. The raw material and packaging material suppliers are qualified by Site QA and Central Quality through vendor assessment procedure as per SOPs.

For all critical materials, suppliers are audited by a vendor qualification team with respect to GMP and regulatory compliance. Such vendors are also continuously monitored and assessed periodically for changes in the qualified system, if any.

1.10 Personnel

Organization organogram

Organization chart (Organogram) was reviewed showing the arrangements for quality management, production and quality control positions/titles up to authorized personnel and senior management.

Training and qualifications

All the departments at the site, including Manufacturing and Development, Quality Control, Engineering and Quality Assurance have enough personnel with appropriate qualifications with respect to education, experience and training to perform the desired functions.

- *Some deficiencies were raised in this section that have been adequately addressed & will be verified in the upcoming inspections.*

Personnel hyiagen

Various hygiene programs were implemented to meet the specific requirements of the factory. Special garments were provided for different classified areas, along with instructions for their proper use, during our inspection we reviewed the Environmental monitoring and personal monitoring and found -no OOS in result of monitoring.

- *Some deficiencies were raised in this section that have been adequately addressed & will be verified in the upcoming inspections.*

1.11Documentation

- *Document control is considered one of the key responsibilities of Quality Assurance. The firm has manual documentation system for recording various manufacturing processes and testing attributes.*

- *All the master documents like Batch records, Standard Testing Procedures, General testing Procedures, Specifications, Qualification documents and Formats are issued, controlled and distributed to users by Quality Assurance Department. Standard Operating Procedures are controlled by Documentum system.*
- *All the filled and completed documents related to product quality (batch records and sequential logbooks) are archived under the control of Quality Assurance Department.*
- *Regardless of process, other supporting documents such as equipment records (operational, cleaning, calibration and maintenance records), facility monitoring records (area cleaning, disinfectant preparation, entry-exit logs, training records, environment monitoring, etc.) are archived under the control of QA.*
- *List of documents was reviewed during inspection and listed in the report.*

1.12 Batch release process

- *The Quality Unit has responsibility for ensuring that all activities associated with manufacturing (purchase, storage, production, quality control, release and distribution) of biologic's are carried out in a systematic and approved manner in compliance with regulatory and GMP requirements*

2. Production

2.1 Drug substance

Good manufacturing practices for pharmaceutical products

- *Live Viral Vaccine Plant (Plant-4) For manufacturing of drug substance of Live Viral Vaccines (Mump, Measles, Rubella,)*
- *(3 laboratories for handling each of Measles, Mumps, Rubella virus separately.) Formulation and filling are carried out in dedicated facility.*
- *Most of Quality Management Systems were operated in a consistent way. These systems are composed of Quality System, Facility and Equipment system, Material System, Production System, Packaging and Labeling System and Laboratory Control System.*
- *The Quality Unit has responsibility for ensuring that all activities associated with manufacturing (purchase, storage, production, quality control, release and distribution) of biologics are carried out in a systematic and approved manner in compliance with regulatory and GMP requirements*

Good practice in production

- *SOPs were in place regarding handling, receiving and transportation of raw material as well as SOPs for release of packaging material.*

2.2 Fill and finishing operations

Fill finish facility (Plant-5/SVP 2) is equipped with formulation vessel, vial washing machine, Depyrogenation tunnel, vial filling and stoppering machine, Lyophilizer, sealing machine, visual inspection booth, labeling machine and packing hall. Dedicated AHU and utilities are available for all the critical activities to avoid the cross contamination.

2.3 Visual inspection

SOP for visual inspection of PFS and liquid /lyophilized vials, cleaning record for visual inspection area & SOP for manual visual inspector qualification program were found in place and reviewed. In addition, Logbook for visual inspection booth, Light intensity measurement record for visual inspection booth, certificate of visual inspector & template for eye examination form for visual inspector in different periods were reviewed as evidence on visual inspection manual and SOP's implementation.

2.4 Process validation

All manufacturing processes were validated and the critical process parameters (CPPs) which affect the critical Quality attributes (CQAs) were clear identified and controlled.

2.5 Reprocessing	*NA*

2.6 Batch manufacturing record

Batch manufacturing record for drug subsnace and for drug product were reviewed during the inspection

3. Facilities and equipment system

3.1 Qualification and validation

Each facility of the site is well equipped with all relevant equipment's based on the process requirement. Once equipment is received in the facility, after initial clearance, a unique ID number is allotted, and all the information of the equipment is maintained in QA as a database. The same are qualified initially and periodically as per criticality of the equipment and process requirements.

- ***Equipment in Manufacturing areas:***

Major equipment includes Roller bottle incubators, CO2 incubators, walk in incubators, Biosafety cabinets, steam sterilizer, Dry Heat Sterilizer, freeze dryer, Laminar Air Flow Cabinets, Fermenters, centrifuges, formulation vessels, filling machines, dehydrogenation tunnel, lyophilizes etc.

- ***Equipment/Instruments of Quality Control areas:***

Major equipment includes steam sterilizer, pH & conductivity meter, TOC analyzer, Analytical balance, dry heat sterilizer, incubators, ultra-fast liquid chromatography, Karl fisher titrator, UV visible spectrophotometers, VITEK 2 etc.

3.2 Calibration

Each facility of the site is well equipped with all relevant equipment's based on the process requirement. Once equipment is received in the facility, after initial clearance, a unique ID number is allotted, and all the information of this equipment is maintained in QA as a database. The same are qualified initially and periodically as per criticality of the equipment and process requirements.

3.3 Maintenance

Regarding maintenance in QC, the engineering department is responsible for the execution of the maintenance activities for ensuring the consistency of the operation of all the systems, utilities and equipment.

3.4 Water system

- *Raw water from bore-well is processed at various stages for particle removal and neutralization and is finally processed through RO system. The purified water is then stored in storage tank and is maintained in constant circulation through mother loop. Dedicated storage tank and secondary distribution systems for purified water are installed at technical areas of each facility.*
- *The secondary distribution loop of purified water also supplies water to dedicated multi column distillation plant for WFI generation. Dedicated WFI storage and distribution systems are installed at technical areas of each facility.*
- *The water generated and circulated throughout the system complies IP, BP and USP*

requirements. Complete water system at each user points is sampled and qualified as per predefined frequency by quality control department. Sanitation of entire loop system done to avoid the formation of biofilm and descaling as per the approved procedure at a predefined frequency.

- *SOP for sanitization of PW storage tank and distribution loop in addition to SOP for sterilization of WFI storage tank and distribution loop and Annual trend analysis of PW 2024 and Annual trend analysis of WFI 2024 there were no excursion in all sampling points, all these documents were reviewed and found satisfactory.*

3.5 HVAC

- *HVAC System and Environmental Monitoring monitored and recorded the critical parameters such as differential pressure (ΔP), temperature, and humidity. Any deviations in these parameters are recorded and managed.*
- *Rooms/laboratory areas in the site are provided with appropriate Heating Ventilation and Air Conditioning (HV AC) system. HV AC system is Recirculation type and designed to take fresh air up to 10%. HVAC system maintains the desired environmental conditions.*
  - *Some deficiencies were raised in this section that have been adequately addressed & will be verified in the upcoming inspections.*

3.6 Aseptic process simulation

- *Process validation at this site ensures that a manufacturing process, when operated within established parameters, consistently produces products that meet their intended use, process validation protocol & the process validation for drug substance and drug products were reviewed and found satisfactory.*
- *The aseptic process simulation was done for the drug substance (annually) and for the drug product it was done twice a year.*
  - *Some deficiencies were raised in this section that have been adequately addressed & will be verified in the upcoming inspections.*

3.7 Cleaning validation

- *The principle of cleaning validation at company was implemented in effective way and Many reviewed documents were well documented and implemented and this also reviewed in deep in previous inspection and during recent one the implementation of validated procedures of cleaning were checked and found no change and no negative impact on production Cleaning validation protocol for product to product change over at LVF facility in addition to Summary report for cleaning verification protocol of product change and there was new Cleaning validation protocol master copy (protocol only) for glass work, stainless steel articles, plastic ware was reviewed and found satisfactory.*

3.8 Storage equipment

Equipment with product-contact surfaces, including vessels, transfer lines, filtration systems, and formulation equipment, is constructed from materials such as SS 316, polypropylene (PP), polycarbonate (PC), or glass, chosen according to product handling requirements. Production equipment is designed for ease of cleaning, employing validated Clean-in-Place (CIP) and Sterilize-in-Place (SIP) systems. Key production equipment for the manufacture of Pneumococcal Polysaccharide (Intermediate), CRM197 (Carrier Protein), Pneumococcal Polysaccharide Bulk Conjugate (Drug Substance), and Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed, 14-Valent) (Drug Product) was available and reviewed during the inspection.

3.9 Computerized system

The company utilizes several validated computerized systems to manage critical parameters effectively.

3.10 Environmental monitoring

Environmental Monitoring monitored and recorded the critical parameters such as differential pressure (ΔP), temperature, and humidity. Any deviations in these parameters are recorded and managed.

- *Some deficiencies were raised in this section that have been adequately addressed & will be verified in the upcoming inspections.*

4. Laboratory control system

4.1Analytical method validation

Quality control is independent and responsible for establishing, validating and implementing all QC procedures, keeping reference samples of material and products, monitoring the stability of the products. QC is responsible for carrying out testing against designed specifications and procedures which should be referenced to pharmacopeia.

- *Some deficiencies were raised in this section that have been adequately addressed & will be verified in the upcoming inspections*

4.2 Out of specifications

The processes for investigating OOS results were evaluated. The laboratory demonstrated a structured approach to OOS investigations, including documented root cause analysis and implementation of corrective actions

4.3 Reference standard

All reference standard storage conditions and certificates of analysis were reviewed and stain history was reviewed and Some deficiencies were raised in this section that have been adequately addressed & will be verified in the upcoming inspections

4.4 Animal house and testing facilities

NA

5. Material system

- *Each consignment of materials after receipt by Warehouse department is initially inspected and batch wisely segregated.*
- *The damaged or improperly labeled containers are separated as "Quarantine" or 'Rejected' and referred to Quality control for further instructions for disposal or return.*
- *Separate areas have been allocated for storage of raw materials and packing materials. Materials are stored at controlled temperature depending upon the storage requirement of the materials. Standard operating procedures for sampling of the raw material and packaging materials are available and followed. Sampling of the raw material is done under Laminar Air Flow Bench. The raw materials are approved or rejected by QC Department based on the results of analysis. Approved materials are stored in Approved Material Storage area in Warehouse.*
- *Printed packaging materials like labels and cartons are stored under lock and key with restricted entry for authorized personnel.*
- *Materials are used in a manner to follow First Expiry First Out (FEFO) basis, or FIFO (First in first out) in case of non-availability of expiry.*
- *Product harvests, concentrates and bulk produced from the respective production areas is stored at its recommended temperature in its dedicated location within the facility under the control of production head. The finished product is stored in cold room at recommended temperature (2°C - 8 °C/ or specified as per shelf-life recommendation).*
- *Arrangements for the handling of rejected materials and products:*
  - Once the incoming material is rejected, it is immediately shifted to "Rejected Material Storage

Area" with red colored "REJECTED" labeling, which is under lock and key. The vendor is informed about the rejection with details of test reports. Quality unit carried out an investigation of the rejected material.

- If the product is rejected at bulk stage, it is decontaminated in autoclaved and then drained into the ETP. If the product is rejected at filled vial stage, all the vials of the batch are decontaminated, crushed and then disposed of. The final disposition details of rejected product are recorded as per written procedures.

6. Packaging and labeling system

Live Viral Vaccine Plant (Plant-4) is designed to manufacture and store concentrated bulk (single harvest) of Measles, Mumps, Rubell and varicella virus in dedicated blocks of Live Virus Production section. The facility is segregated based on the process activity such as media preparation, normal cell culture area, virus culture lab (4 laboratories for handling each of Measles, Mumps, Rubella and varicella virus separately.) Formulation and filling are carried out in dedicated facility. Fill finish facility (Plant-5/SVP 2) is equipped with formulation vessel, vial washing machine, Depyrogenation tunnel, vial filling and stoppering machine, Lyophilizer, sealing machine, visual inspection booth, labeling machine and packing hall. Dedicated AHU and utilities are available for all the critical activities to avoid the cross contamination. The facility is approved by FDCA, Gandhinagar. The labelling and packaging machines were qualified.

Part 3	**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 life sciences limited vaccine technology center) 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, Tai: Sanand, Dist.- Ahmedabad - 382 213), was considered to be operating at an acceptable level of compliance with WHO good manufacturing practices for biological products guidelines.*
- *All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the EDA-PIR, were addressed by the manufacturer, to a satisfactory level, prior to the publication of the EDA-PIR*
- *This EDA-PIR will remain valid till next inspection, as long as there is any warning or recall from SRA.*

Part 4	**List of GMP 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-eight Report Geneva, World Health Organization, 2014*

Short name: WHO TRS No. 986, Annex 2

https://www.who.int/publications/m/item/trs986-annex2

2.*WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010*

Short name: WHO TRS No. 957, Annex 2

https://www.who.int/publications/m/item/annex-2-trs-957

3.*WHO guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report. Geneva, World Health Organization, 2018*

Short name: WHO TRS 1010, Annex 9

https://www.who.int/publications/m/item/trs1010-annex9

4. *WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021*

Short name: WHO TRS No. 1033, Annex 3

https://www.who.int/publications/m/item/annex-3-trs-1033

5.*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*

Short name: WHO TRS No. 929, Annex 4

https://www.who.int/publications/m/item/annex-4-trs-929

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*

Short name: WHO TRS No. 957, Annex 1

https://www.who.int/publications/m/item/trs957-annex1

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*

Short name: WHO TRS No. 957, Annex 3

https://www.who.int/publications/m/item/trs957-annex3

8.*Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty Second Report Geneva, World Health Organization, 2018*

Short name: WHO TRS No. 1010, Annex 8

https://www.who.int/publications/m/item/Annex-8-trs-1010

9.*Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditionning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Third Report Geneva, World Health Organization, 2018*

Short name: WHO TRS No. 1019, Annex 2

https://www.who.int/publications/m/item/trs1019-annex2

10. *WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2022*

Short name: WHO TRS No. 1044, Annex 4

https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/production/trs1044-annex4-technology-transfer-in-pharmaceutical-manufacturing.pdf

11. *WHO good manufacturing practices for sterile pharmaceutical products. Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.*

Short name: WHO TRS No. 1044, Annex 2

https://www.who.int/publications/m/item/trs1044-annex2

12. *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*
Short name: WHO TRS No. 943, Annex 3
https://www.who.int/publications/m/item/trs943-annex3
13. *WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011*
Short name: WHO TRS No. 961, Annex 2
https://www.who.int/publications/m/item/trs961-annex2
14. *WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013*
Short name: WHO TRS No. 981, Annex 2
https://www.who.int/publications/m/item/trs981-annex2
15. *WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013*
Short name: WHO TRS No. 981, Annex 3
https://www.who.int/publications/m/item/annex-3-trs-981
16. *WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011*
Short name: WHO TRS No. 961, Annex 14
https://www.who.int/publications/m/item/tr961-annex14
17. *Good Manufacturing Practices: Guidelines on validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Third Report Geneva, World Health Organization, 2019*
Short name: WHO TRS No. 1019, Annex 3
https://www.who.int/publications/m/item/trs1019-annex3
18. *WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015*
Short name: WHO TRS No. 992, Annex 4
https://www.who.int/publications/m/item/trs992-annex4
19. *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*
Short name: WHO TRS No. 961, Annex 9
https://www.who.int/publications/m/item/trs961-annex9-modelguidanceforstoragetransport
20. *WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015*
Short name: WHO TRS No. 992, Annex 5
https://www.who.int/publications/m/item/trs992-annex5
21. *WHO Recommendations for quality requirements when plant – derived artemisinin is used as a starting material in the production of antimalarial active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015*

Short name: WHO TRS No. 992, Annex 6
https://www.who.int/publications/m/item/trs-992-annex-6

22. *Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2021*
Short name: WHO TRS No. 1033, Annex 4
https://www.who.int/publications/m/item/annex-4-trs-1033

23. *WHO general guidance on variations to multisource pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report Geneva, World Health Organization, 2016*
Short name: WHO TRS No. 996, Annex 10
https://www.who.int/publications/m/item/trs966-annex10

24. *Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Second Report Geneva, World Health Organization, 2018*
Short name: WHO TRS No. 1010, Annex 10
https://www.who.int/publications/m/item/trs1010-annex10

25. *Points to consider when including Health-Based Exposure Limits in cleaning validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2021*
Short name: WHO TRS No. 1033, Annex 2
https://www.who.int/publications/m/item/annex-2-trs-1033

26. *Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fourth Report Geneva, World Health Organization, 2020*
Short name: WHO TRS No. 1025, Annex 6
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