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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Active Pharmaceutical Ingredient Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**Tianish Laboratories Private Limited (Unit-8)**
Corporate address of manufacturer	Plot No. 564/A/22, Road No. 92, Jubilee Hills, Film Nagar, Shaikpet, Hyderabad – 500 034, Telangana, India.
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Tianish Laboratories Private Limited (Unit-8) G. Chodavaram, Poosapatirega Mandal, Vizianagaram District 535 204, Andhra Pradesh, India. D-U-N-S: 650438158 GPS: Latitude, longitude: 18°06'51.88" N, 83°34‘42.68" E

Synthetic unit /Block/ Workshop

Product Name	**Building**	**Workshop**
Efavirenz	MB-1, 4, 5, 9 & 15	MB-4 Module-1, MB-9 Module-1 & Module-2, MB-5 MB-01 Module-III and MB-15
Ritonavir Form-II	MB-5 MB-1,4,12 & 15	MB-5, MB-4, MB-12, MB-15 Module-2
Tenofovir Disoproxil Fumarate	MB-1, 15, 10, 9 & 8	MB-10 Module-1 & Module-2, MB-8, Module-2 MB-1 Module-III, MB-9 Module-1, and MB-15
Abacavir Sulfate	MB-2,4,5, 1, 15	MB-1 Module-1, MB-2, MB-4, MB-5, MB-15
Lamivudine intermediate	MB-1	MB-1 Module-1, Module-5 & Module-6
Daclatasvir Dihydrochloride	MB-6 MB-1 & MB-15	MB-6 Module-II MB-1- Module-III & MB-15
Emtricitabine - Intermediate	MB-1 MB-3 MB-2 MB-4	MB-1 Intermediate MB-3 Intermediate MB-2 and MB-4
Sofosbuvir	MB-6 MB-1,7, 3 & 15	MB-6 Module-II, MB-1 & Module-II & MB-15
Bedaquiline Fumarate	MB-6 & 1	MB-6 Module-I and Module-II, MB-1
Delamanid	MB- 6 & 3	MB-6 Module 1 &2 and MB-3

	Delamanid SD Powder	MB-14 & 15	MB-14 MB-15
	Velpatasvir	MB-6,1 & 15, 3, 8	MB-6 Module-1 & Module-2 and MB-3, MB-8, MB-1 Module-1 and MB-15

Dates of inspection	22-26 January 2024
Type of inspection	Routine GMP inspection
Introduction	
Brief description of the manufacturing activities	The manufacturing facility, Unit-8, was established in 1993. Previously known as M/s Vera Laboratories Limited, it was acquired by Matrix Laboratories Limited in 2004. In 2007, Matrix Laboratories Limited was acquired by Mylan Inc., USA. The company was renamed "Mylan Laboratories Limited (Unit-8)" in 2011. Mylan Laboratories Limited has demerged its API business to Tianish Laboratories Private Limited, effective March 01, 2024. Unit-8 manufactures intermediates, active pharmaceutical ingredients, and active pharmaceutical ingredient premixes for domestic and international market supply.
General information about the company and site	Tianish was founded in 2023. The company primarily produces active pharmaceutical ingredients and has a corporate office in Jubilee Hills, Hyderabad, India.
History	Unit-8 has been regularly inspected by the WHO Prequalification Inspection Services. The last inspection was conducted in November 2019. This facility has been inspected by various Regulatory agencies / Health authorities (USFDA, PMDA, AGES, COFEPRIS, CDSCO, Russian GMP, ANVISA, EMA and TGA). The following major changes were made since the last WHO PQ inspection: - New facility created and qualified at MB-01 (Module 6) - March 2020 - New Sampling/ Dispensing booths facility commissioned and qualified for Amines/Amides at Raw Material Warehouse- 4 & 5 - August 2020 - New intermediate block commissioned and qualified as Manufacturing Block (MB-12) - November 2020 - New Solvent recovery plant (SRP-3) commissioned and qualified - February 2022 - New Manufacturing Block-14 commissioned and qualified - November 2022.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	The following areas were inspected: - Quality management system - Personnel and training - Buildings and facilities - Qualification and validation - Production and packaging operations - Quality control laboratories

	- Warehouse - Utilities
Restrictions	None
Out of scope	The inspection was limited to the APIs submitted for Prequalification. Other APIs and intermediates were excluded from the inspection.
WHO APIs covered by the inspection	Sofosbuvir Daclatasvir dihydrochloride Abacavir sulfate Tenofovir disoproxil fumarate Emtricitabine Ritonavir Form-II Lamivudine intermediate Efavirenz Velpatasvir Delamanid Bedaquiline Fumarate Delamanid SD Powder
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
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
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
KF	Karl Fisher
LAF	Laminar airflow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory

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
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer

Part 2	**Summary of the findings and comments**

1. Quality management

The quality unit comprised quality assurance and quality control and was independent of production. The job descriptions of the persons authorized to release intermediates and APIs were specified. The deviations were handled following an approved procedure. The materials were released before being used to manufacture intermediates and APIs. The manufacturing site has been using the following software applications for quality management:

S. No.	System	Used for
1	e1 SAP	Material Management, Batch Release, Manufacturing Process Equipment Logbook, Equipment Preventive Maintenance
2	TrackWise	QMS Elements (Incidents, Change Controls, Investigations, Complaints and CAPA)
3	LIMS	Laboratory Sample and Data Management
4	Empower3	Chromatography (HPLC, GC)
5	Documentum D2	Master Batch Production Record (MBPRs) and Standard Operating Procedure (SOPs)

6	MyUniversity	Training

The following quality management elements were reviewed:

The SOP for product quality review was reviewed and applied to all APIs and intermediates manufactured at Tianish sites. Based on the follow-up action, the procedure stated that it would be concluded if it was a Level I, II, or III classification of PQR. The PQR was performed for the batches manufactured during the previous calendar year and had to be completed by the end of February. The procedure stated that trend analysis would be performed when 12 or more batches would be manufactured, where less than 12 batches would be manufactured, and graphs and control charts would be prepared for guidance. The PQR included reviews of packaging materials, change controls, out-of-specifications (OOS), API starting materials, critical quality parameters, intermediate manufacturing review, critical process parameters, in-process controls, incidents, process validation, reprocessing, reworking, rejection, recovered solvents, and final API review, complaints, returned goods, product recall, stability study data, retention samples etc. The process capability (Ppk) was performed using Minitab, and a minimum of 25 batches were required. The Ppk of 1.33 or more (4 sigma level) was considered favorable, whereas between 1.00 and 1.33 (3 to 4 sigma) was also acceptable. If Ppk was reported below 1.0, an investigation would be performed, and appropriate action would be initiated. In general, the procedure was found adequate. During the inspection, APQRs for the review period Jan-Dec 2023 were still under preparation for all WHO APIs.

The quality risk management procedure was reviewed. It provided instructions on performing a risk assessment. It was a corporate procedure applied at all Tianish sites. The company used FMEA and RPN to assign risk (high, medium, or low). The risk assessment was performed and documented.

The SOP on handling and investigating incidents/deviations were reviewed, and the scope included manufacturing activities. It did not apply to the laboratory, covered under a separate SOP (laboratory investigation report). The deviation was a corporate procedure applicable to all Tianish API sites. Deviation/incident reporting was handled through TrackWise software and recorded on the BMR's page. An impact assessment was performed for each incident report, and the report was closed out if the root cause and CAPA were fully documented and no impact on product quality was foreseen. There were two types of incident categories: manufacturing incidents relevant to OOT/OOS linked to product non-compliance and operational incidents covering all other manufacturing-related incidents. A product impact assessment categorized the impact as severe, major, medium, minor, or negligible. Incident reports were classified based on risk to critical, major, or minor. Minor operational deviations should be closed after 12 days, and all other deviations should be elevated to the investigation report and closed within 45 days. In 2023, 34 incident reports were registered in TrackWise software. All incident reports were classified as minor.

The SOP for management review was discussed, and it was noted that MR was conducted once every two months. The QA prepared a schedule with tentative meeting dates before the start of the new year. The annual schedule of management review for 2023 was reviewed and found to be scheduled on a quarterly basis, and meetings were held as scheduled. The last management review conducted on 18/11/2023 was reviewed, including the attendee's list and agenda. The meeting included reviewing many quality indicators for the review period Sep - Oct 2023.

The SOP of the internal quality audit was reviewed. The internal audit plan was prepared by the QAD within 30 days of the beginning of the year; at least 2 internal audits had to be conducted every year for each department. CAPA should be submitted within 15 Working days. Inspection checklists were used for each department. The internal audit (Self-inspection) annual schedule for 2024 was available. The schedule for 2023 was reviewed, and self-inspection was carried out as scheduled. The updated list of internal auditors (1/2024) was reviewed. MB-1 was planned to be inspected on 7 April 2023 for 2 hours by two qualified auditors who conducted the inspection.

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

2. Personnel

The site had adequate personnel to perform and supervise the manufacture of intermediates and APIs. From the opening meeting presentation, it was noted that 1048 personnel were on the company's payroll. In addition, approximately 1000 contracted workers were employed to conduct various tasks. The staff were knowledgeable and qualified. Job descriptions of staff were in place. The job description of the QA officer was reviewed, and it found that API release and dispatching activities to market, as well as handling returned goods, were assigned to him on 23/6/2021.

The SOP for employee training was reviewed**.** It was a corporate procedure applicable to all Tianish API sites. The training calendar was prepared annually. The training was managed through a Learning management system application called My University. The annual training schedule for 2023 and its implementation were reviewed. Every department was divided into different training groups based on their Job profile. A training curriculum was planned for each group on the number of SOPs and 2 annual training modules for GMP -ICH Q7 and data integrity. Annual Training plans were prepared for 2024. The annual Training plan prepared for 2023 was reviewed. Job-specific training on SOPs was done through the Myuniversity software application. Annual GMP -ICH Q 7 and data integrity training plans were conducted face to face. Training records of G. Sandeep Kumar Raju, the authorized person for release and dispatch, were extracted from the Myuniversity application and reviewed.

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

3. Buildings and facilities

Unit-8 was spread over 68.2 acres and consisted of 14 Manufacturing Blocks (MB) and 3 solvent recovery plants (SRP). In addition, Unit-8 was equipped with three quality control laboratories, two purified water plants, two finished goods warehouses, a process development lab, five raw material warehouses (liquid and solid), one packaging material warehouse, nine utility blocks, and two effluent treatment plants. It was noted that Unit-8 manufactured 78 products, including intermediates and finished APIs. MB 12 was commissioned in November 2020, and MB 14 in November 2022. In MB-1, a new pharma area (Module 6) was created in March 2020. HVAC systems were placed on the upper level of each building. All pharma areas (finished API manufacturing area) were classified as Grade D. Solvent recovery plant SRP -3 was recently constructed in Feb 2022. New sampling and dispensing areas were

commissioned to raw material warehouses 4 & 5 in August 2020. There were 3 Quality control laboratories, where QC labs 1 and 3 were used for testing raw material, in-process control, and recovery of solvent samples. QC lab 2 was used to test the finished API.

MB-1, 3, 5, and 14 were inspected. Overall, temperature and humidity were not monitored in all intermediate manufacturing areas. The MB-5 building, and all equipment were well-maintained, including the pharma areas (finished API manufacturing area) of buildings 1, 3, and 6B.

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

4. Process equipment

Unit-8 was equipped with various process equipment such as stainless-steel reactors, glass-lined reactors, centrifuges, spray dryers, vacuum tray dryers, rotary cone vacuum driers, multimill, sifters, agitated nutche filter dryers, candy filters, leaf filters, nutche filters, micron filter and more. The site was sporadically using closed or contained equipment, such as a pressure transfer system for transferring materials into the reactors. Where materials were charged through a manhole, the adjacent reactors were closed. All Equipment had QR codes, which, upon scanning by a RIF gun, opened an E-log for equipment, where manufacturing & cleaning activities were recorded. Reactors were found to have Equipment data cards displaying all data relevant to qualification, calibration, and maintenance. Other equipment, e.g. centrifuges, AF, millers, sifters, and driers, did not have the same Equipment data card. Although equipment maintenance, calibration, and cleaning schedules were maintained through the SAP system, no qualification/calibration/ maintenance label was affixed to the reactors. In general, non-dedicated equipment were used with some exceptions. Cleaning validation was performed for shared equipment following the health-based exposure limit requirement. The site uses several computerized systems for quality management and product manufacturing. Some computerized systems have not been adequately validated, as noted from the review of the documents. Also, the site has recently started using SCADA/HMIs to manage recipes.

The SOP for preventive maintenance process equipment was reviewed. After preparing PM schedules, dates were entered into the SAP system, and PM orders were generated automatically 15 days before the due date. According to a preventive maintenance matrix, maintenance was conducted quarterly, half-yearly, and annually for different equipment.

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

5. Documentation and records

The documents, such as Standard Operating Procedures and Master Batch Production Records (MBPR), were prepared using Documentum D2. During the site tour, it was noted that the approved procedures and instructions could be accessed through monitors in read/view mode. Upon review of several SOPs, it was noted that the SOPs were provided with a revision history. The manufacturing batch production record for Delamanid SD powder and the Master Manufacturing Document were reviewed. The

production personnel prepared and verified these documents by the QA before being uploaded onto the SCADA/HMI.

The SOP for the release of intermediates and APIs to customers was reviewed. The list of authorized personnel to release dispatched batches was reviewed and found to have 11 QA personnel.

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

6. Materials management

The written procedures described handling incoming materials, including receipt, storage, sampling, and testing. The SAP system was used for material management. Raw materials (RM) were stored in five (5) warehouses: 3 for liquid raw material RM (RM WH 1, 4 & 5), and 2 for solid RM (RM WH 2 & 3). Finished goods were stored in 2 warehouses, whereas packaging materials (PM)were stored in the PM warehouse. Materials were managed through the SAP system. RM warehouse 2 for solids RM and FG warehouse 1 were inspected. Temperature and relative humidity were monitored. Finished goods warehouse 1 consisted of 2 floors: the ground floor for final APIs & first floor for pre-mix RM [e.g. Delamanid]. In RM warehouse 2 for solids RM, there were 2 sampling & dispensing rooms and 1 hazardous material room. There was one walk-in cold storage room 2-8°C, which was monitored for temperature through data logging software. The returned goods area was found in the FG -3 warehouse.

The SOP for handling returned goods was reviewed. Upon receiving returned goods, the business development department (BDD) created a return sales order. The returned products were stored in segregated and locked areas and placed under hold status on SAP. Goods were inspected using a checklist, and testing could be decided based on the QA decision along with any further investigations.

The SOP for evaluating and approving suppliers of API starting material, general RM, and packaging material was reviewed. The procedure was applicable for API SM supplied from other Tianish internal sites. For purchasing from contract manufacturing units (CMU), Tianish followed another procedure of the CMU management. There were 11 starting materials for 12 APIs under the scope of inspection. A list of qualified suppliers for all SMs was available.

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

7. Production and in-process controls

The inspectors visited the manufacturing block MB-6B. It was noted that Delamanid API small-scale batches were manufactured in MB-6A, and large-scale batches were manufactured in MB-6B. The building consisted of three floors. The ground floor included the centrifuges area, the powder processing area, and the pharma area. On the first floor, several reactors were installed, and the second floor housed reactors and dryers. At the time of the visit to the 6B area, Velpatasvir was being produced. The batch manufacturing record was available near the reactor. Equipment such as reactors, charge tanks, agitated filters, centrifuges, vacuum tray dryers, multi-mill, rotary cone vacuum dryers, micron filters, blenders, and sifters used for the manufacturing of Delamanid API was verified against the approved manufacturing process. Generally, the names and direction signs were provided for various lines and utilities. The materials were charged mostly through the manhole of the reactors. In contrast, a pressure

transfer system was used only in a few steps where Tenofovir Stage II was manufactured. Batch-to-batch cleaning of the reactors and filters was performed. For micron filters, visual integrity was verified and replaced every 15 batches.

The MB-14 (new block established to increase manufacturing capacity) was visited for Delamanid Spray Drying Powder. The spray drying process was carried out inside the Grade D classified area. At the time of the visit to the area, Delamanid Batch No. 20174855 was being produced. The spray dryer close loop system was equipped with Human Machine Interface, which used a recipe to process the spray drying. Delamanid API was charged through the manhole of the reactor, whereas dichloromethane and ethanol were charged through respective solvent lines after passing through the micron filters (0.22µm). After the dissolution process, the material was filtered through a candle and micron filters before being transferred to the reactor. The semi-dried material was collected in an SS collection bin before being transferred to a blue drum containing white LDPE and black LDPE. After weighing, the material was transferred for drying through a pass-box. The drying was carried out in the adjacent module II. Module II was equipped with an airlock, changeroom, buffer room, and 2 vacuum tray dryers and sifters. Finally, the material was packed and transferred through the exit.

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

8. Packaging and identification labelling of APIs and intermediates

APIs were packaged inside the Grade D environment of the Pharma area using a hot sealing machine. Three WHO APIs (RIV-form II, RIW), Tenofovir disoproxil fumarate, and Velpatasvir were packed under nitrogen, which was produced in-house from a nitrogen production plant.

Ritonavir was packed in an antistatic white low-density polyethylene bag [LDPE] under nitrogen and sealed, placed in a black PE bag and hot-sealed, and placed in a triple polyester film aluminium bag and hot-sealed. Finally, it was transferred to an HDPE drum, which was closed and sealed. The normal pack size was 25 Kg, and food-grade primary packaging material was used.

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

9. Storage and distribution

Adequate facilities were available for the storage of incoming and in-process materials. Upon reviewing the day-store area in the manufacturing blocks, it was noted that adequate segregation was not provided to ensure that different materials and batches of the same materials were not mixed up. Dataloggers were attached to the consignment before dispatch from the manufacturer. The data logger calibration range was from -30°C to +70°C. The Calibration certificate of one of the dataloggers was reviewed.

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

10. Laboratory controls

The quality control laboratory (QCL) was visited in the afternoon of day 3. A total of three QCLs supported various production activities. QCL 1 performed testing related to in-process samples, raw materials, intermediates, and microbiology. QCL 2 performed finished product/API testing and stability studies spread over the ground and first floors. QCL 3 also performed testing to support the 14 manufacturing blocks. The specifications and test procedures for Delamanid, Delamanid Spray Dried Powder, and Bedaquiline Fumarate were reviewed.

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

11. Validation

The validation master plan provided guidance for conducting validation activities for Unit-8. The VMP covered equipment qualification, process validation, cleaning validation/verification, utilities, air handling units, water systems, analytical method validation and computerized system validation etc. The company had introduced 22 new APIs since the last PQ inspection in 2019. The assessment sheet for cleaning validation (new API introduction)- Delamanid was available. Similarly, assessment sheets for Delamanid Spray Dried Powder (MB-14, dated 05/01/2023) and Bedaquiline Fumarate were available. These assessment sheets confirmed that existing controls were adequate from a cross-contamination point of view; hence, these new APIs can be processed in the manufacturing blocks. Similarly, the company prepared the assessment sheets for the remaining molecules introduced since the last PQ inspection.

Cleaning validation, process validation, analytical method validation, and other validation activities were carried out according to the respective SOPs and protocols.

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

12. Change control

A formal change control (CC) system was established to evaluate changes, and TrackWise was used. The SOP of the change management process was reviewed and noted that it was a corporate SOP applied to all Tianish sites and all manufacturing activities. The CC was managed through the TrackWise software program. There were 1485 CCs initiated in 2023; 35 were classified as critical and 326 as major. 10 critical CCs were still under implementation.

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

13. Rejection and re-use of materials

The site had specific procedures for managing rejection, re-use, returns, solvent recovery, reprocessing, and reworking activities.

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

14. Complaints and recalls

The SOP for handling customer complaints was reviewed and noted as a corporate SOP for investigating and managing quality complaints. Upon receipt by the business development BD or corporate quality department, it was directed to the head of site quality within 3 business days for further action. Complaints were classified as critical, major & minor quality defects/complaints. Trending of complaints was done on a quarterly basis. Complaints were managed through the TrackWise software program, which included electronic signatures. A risk assessment was done within 2 days of receiving the complaint. Further notification and actions should be taken within the timelines for critical complaints. Investigation of critical complaints should be completed within 15 days; other complaints should be investigated within a 45-day timeline. Further to root cause identification, CAPA should be initiated.

The SOP for product recall was applied for all APIs manufactured by Tianish company as well as post-marketed finished products manufactured utilizing Tianish API. The Head of global OSD & API quality was responsible for deciding on a recall. Recalls were classified as I, II & III. A recall letter will be sent to the consignee within 3 business days of the recall committee's decision. The procedure stated that the recall effectiveness could be checked, but no timeline was assigned for each type as per risk. A mock recall was conducted based on the worst-case risk evaluation every 3 years +/- 1 month. No recall was performed for APIs manufactured at Tianish U-8. The last Mock recall was conducted on 23 Dec, 2020.

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

15. Contract manufacturers (including laboratories)

The company confirmed no contract manufacturing was carried out for any WHO PQ products. Since the last PQ inspection in 2019, the company had introduced another solvent recovery plan to recover the solvents within Unit-8. Some of the analytical tests were outsourced to Unit-8.

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, ***Tianish Laboratories Private Limited***, located at ***G. Chodavaram, Poosapatirega Mandal, Vizianagaram District 535 204, Andhra Pradesh, India*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines for APIs.

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 GMP Guidelines referenced in the inspection report**

1. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2. ***Short name: WHO TRS No. 957, Annex 2***
   http://www.who.int/medicines/publications/44threport/en/

2. 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***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

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
   http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

4. 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

5. 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
   http://www.who.int/medicines/publications/44threport/en/

6. 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
   http://www.who.int/medicines/publications/44threport/en/

7. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Sixth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 1044), Annex 2.
Short name: WHO TRS No. 1044, Annex 2
TRS 1044 - Annex 2: WHO good manufacturing practices for sterile pharmaceutical products

8. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Sixth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 1044), Annex 4.
Short name: WHO TRS No. 1044, Annex 4
TRS 1044 - Annex 4: WHO guidelines on technology transfer in pharmaceutical manufacturing

9. 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 9***
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

10. 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
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

11. 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***
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

12. 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***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

13. 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***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

14. WHO Guidelines on good manufacturing practices: validation, Appendix 7: non-sterile process validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 3. ***Short name: WHO TRS No. 992, Annex 3***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

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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