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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
Quality Control laboratory

Part 1	**General information**
Laboratory Details	
Name of the laboratory	Drugs Testing Laboratory Punjab, Multan (DTLM)
Address of inspected laboratory	Drugs Testing Laboratory Punjab, Multan (DTLM) Near Kidney Center Muzaffar Ghar Road, Multan, Punjab Pakistan
GPS coordinates	Longitude: 30.1398294 Latitude: 71.4773698
Address of corporate office, telephone number and fax number	Same as above
Dates of inspection	7 - 9 December 2022
Type of inspection	Initial
Introduction	
Brief description of testing activities	

Type of analysis	**Finished products**	**Active Pharmaceutical Ingredients**
Physical/ Chemical analysis	pH, Extractable volume, Disintegration, Dissolution, Conductivity, Weight variation of tablet and capsule, Testing of c otton products (Weight per unit area, Sinking time, W ater holding capacity, W arps and wefts, A cidity and alkalinity)	pH, Water content, Loss on Drying, Density, Melting point, Conductivity
Identification	HPLC (PDA, FLR, RI), UV-Visible spectrophotometry, FTIR	HPLC, TLC, Spectrophotometry (UV-Visible and FTIR)
Assay, impurities, and related substances	Assay by HPLC (PDA, FLR, RI), UV-Visible spectrometer, UHPLC, FTIR, Potentiometric titration and other titrations, Related substances, and impurities	Assay by HPLC (PDA, FLR, RI), UV-Visible spectrometer, UHPLC, FTIR, Potentiometric titration and other titrations, Related substances and impurities

General information	DTL Multan is a legal entity and part of the Government of Punjab and established with order No. PO (D-II) I -90/2008 and was upgraded and revamped in 2016. DTL, Multan is a project of Government of Punjab, established under the Drug Act 1976 and its regulatory body is PQCB (Provisional Quality Control Board), Government of Punjab. The laboratory is headed by Director who has overall responsibility of operations and provision of resources needed to ensure the required quality of the laboratory. Drugs Testing Laboratory, Multan is located in 24,000 square feet piece of land situated on the site of the newly constructed DHQ Hospital/Kidney Center at Muzaffargarh Road Multan. DTL Multan provides services of pharmaceutical testing of drug samples. Provincial Quality Control Board (internal customer of the laboratory) is the designated body in the Drug Control Wing of the Department, which has technical capabilities and legal function to scrutinize test reports, audit and suggest improvements in the Drugs Testing Laboratories. Preference is given to use reference methods published by the pharmacopoeias in order of the preferences given in the Drugs Specifications Rules 1978 notified under the Drugs Act 1976. When necessary, the standard can be supplemented with additional details to ensure consistent application. In DTL Multan, if customer does not specify the method to be used, laboratory-developed methods or methods adopted by the DTL Multan may also be used if appropriate for the intended use and if validated. The laboratory confirms that it can properly operate methods before applying them to samples. The DTL Multan uses test methods that meet the needs of the customer and are appropriate for the tests it undertakes.
History	This was the first inspection carried out by WHO Prequalification team. The Drugs Testing Laboratory Punjab, Multan has been accredited by Pakistan National Accreditation Council on ISO/IEC 17025 - The Laboratory Accreditation Certificate Number is LAB:160.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Quality Management System Personnel Training and Safety Documentation and Records Premises and Equipment Validation - Qualification - Calibration Laboratory Practices Reference standards - Reagents - Water
Restrictions	N/A
Out of Scope	Microbiology Laboratory

Abbreviations	Meaning
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
BP	British Pharmacopoeia
CS	Computerized system
CoA	Certificate of analysis
CAPA	Corrective action & Preventive action
DQ	Design qualification
FPP	Finished pharmaceutical product
FTIR	Fourier transform infrared spectrophotometry or spectrophotometer
GC	Gas chromatography or Gas chromatography equipment
GLP	Good laboratory practice
HPLC	High-performance liquid chromatography (or high-performance liquid chromatography equipment)
IQ	Installation qualification
IR	Infrared spectrophotometry
ISO	International Standards Organization
KF	Karl Fisher titration
LIMS	Laboratory information management system
MB	Microbiology
MR	Management review
N	Normality
NC	Non-conformity
OOS	Out-of-specifications test result
OQ	Operation qualification
Ph. Eur.	European Pharmacopoeia
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PT	Proficiency testing
PTS	Proficiency testing scheme
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QM	Quality manual
QMS	Quality management system
QRM	Quality risk management
QS	Quality system
RA	Risk assessment
RCA	Root cause analysis
SOP	Standard operating procedure

TLC	Thin layer chromatography
TOC	Total organic carbon
UPS	Uninterruptible power supply
URS	User requirements specifications
USP	United Stated Pharmacopoeia
UV	Ultraviolet-visible spectrophotometry or spectrophotometer
VMP	Validation master plan
VS	Volumetric solution

Part 2	**Summary of findings and recommendations**

1. Organization and management

Drugs Testing Laboratory Punjab, Multan (DTLM) was legally authorized to function and can be held legally responsible. DTLM had managerial and technical personnel with the authority and resources needed to carry out their duties and had arrangements to ensure that its management and personnel are not subject to commercial, political, financial and other pressures or conflicts of interest that may adversely affect the quality of their work.

DTLM had in place an organizational chart which depicted the organization and management structure of the laboratory.

2. Quality management system

The management system was explained in the following documents:

- Quality Manual
- Quality Policy Statement
- SOPs (Procedural SOPs and Equipment SOPs

DTLM had established, implemented, and maintained a quality management system appropriate to the scope of its activities and had established, implemented, and maintained authorized written SOPs. The activities of the DTLM were systematically and periodically audited internally and externally. Management review of quality issues were regularly undertaken.

DTLM has participated in proficiency testing programs on a regular basis. QA plan for proficiency testing was provided to inspectors. DTLM participated in following tests:

- Disintegration
- Weight variation
- Dissolution
- HPLC
- Advance titration/acid base titration
- Sterility
- Refractive index
- Melting point

- UV
- pH
- Conductivity
- Endotoxin test
- Uniformity of weight

QMS Master Plan

"QMS Master Plan" was available and specified:

- Supplier qualification
- QA plan
- Internal audit plan
- Electronic data back-up plan
- MR meeting plan
- Customer feedback plan
- Training need assessment plan
- Weekly analytical work plan
- Safety drill

Management review (MR)

Management reviews were performed in accordance with SOP "Management Review Meeting". Purpose of this SOP was to ensure a suitable and effective laboratory management system is implemented to provide better drug testing services, review the laboratory's quality management system, and bring necessary changes or improvements in drug testing services, including testing and management activities.

MR meeting of Quality System was conducted annually as per agenda. MR meeting was held to examine the QS and to determine if the QS meets the conditions set by the laboratories and the standards.

MR meeting schedule was circulated one week prior to the meeting to all prospective participants. Schedule specified MR meeting agenda points to be covered along with date and time. MR meeting was chaired by Director. Standard agenda was specified.

Meeting minutes were recorded by QMS Manager or assigned person. Minutes included decisions made and or corrective/preventive actions taken on the agenda items. Meeting minutes were circulated to all managerial personnel and signed within ten days from the date of the meeting.

Complaints

Handling of complaints was explained in SOP "Standard Operating Procedure for Complaints Management". Complaints were internal and external. Complaints were received and recorded by QMS Manager on complaint form. Register from 2021 to date was presented.

Data integrity
Data integrity was explained in "Standard Operating Procedure for Data Integrity". This procedure was applicable to all controlled documents, protocols, reports, and equipment data of DTLM. SOP explained ALCOA+ principles. Date and Time function of chromatographic systems was locked.
Password Policy was explained in SOP "Standard Operating Procedure for Computer System Validation".

Computer System Access and Password Policy
Procedure for Computer System Access and Password Policy was explained in SOP "Standard Operating Procedure for Computer System Validation".

Data Back-up and Restoration
Data back-up and restoration was explained in SOP "Standard Operating Procedure for Control of Records". Electronic data back-up plan was available.

Change control
Change management was performed in accordance with SOP "Change Control Management". The SOP applied to specifications/methods for analytical tests, reporting, analytical method validation, equipment qualification, preventive maintenance of equipment's, any modification which was planned for alteration, deletion, up-gradation, repair and replacement of equipment, facility, area, or utility.

Changes were categorized as:
- Critical
- Major
- Minor

Change Control Logbook and a number of Change Controls were reviewed.

Handling of non-conformances (deviations)
Handling of non-conformances (NC) was described in the SOP "Control of Non-Conforming Work/Deviation".

SOP was applicable to all the sections of Drugs Testing Laboratory, Multan. The purpose was to prevent or handle any non-conformity in any section, to improve the quality management system, and to meet requirements of International Standards Organization ISO 17025: 2017.

Non-conformities were classified as:
- Critical
- Major
- Minor
- Observation

Non-Compliance Information Log Book and a number of non-conformances were reviewed.

Corrective actions(CAPA) and Root Cause Analysis (RCA)
Corrective actions were described in the SOP "Standard Operating Procedure for Corrective Action".

Problems highlighted within the management system or technical operations were reported by identifying person. When a problem was identified, the responsible person performed root cause analysis of the non-conforming work. The following tools were used for RCA:

- Fishbone diagram
- 5 Whys
- Impact analysis

Risk Management system
Risk assessment was described in SOP "Risk assessment". Risk was calculated through FEMA (Failure Effect Mode Analysis) by calculating Risk Priority Number (RPN), Risk Level was assigned as High, Medium, and Low.

Internal audits
SOP "Internal Audit" was aligned with ISO 17025 and WHO Guidelines. Internal audit was conducted biannually according to audit plan. A documented audit schedule was prepared by the QMS Manager or Deputy QMS and approved by the Director. In most cases, QMS Manager was Lead Auditor. Lead Auditor was trained on standards to conduct the internal audit. After audit, auditors should report nonconformities within one week. Laboratory management should submit Action Plan within maximum of two weeks. Follow up audit to evaluate corrective actions was performed by audit team.

Audit findings were classified:

- Critical non-conformance
- Major non-conformance
- Minor non-conformance
- Observation

External audits
List of external audits were performed from 2020 was presented.

Procedure "Continuous Improvement" and trends related to opportunities for improvement were discussed.

3. Control of documentation

DTLM had established and maintained procedures to control and review all documents that form part of the quality documentation. A master list identifying the current version status and distribution of documents was established and was readily available.

SOP"Standard Operating Procedure for Document Control" required documents to be updated/revised as per the review date. Periodic revision was done every 2 years. Relevant staff were trained on new and revised SOP prior to the effective date of the SOP.

Documents had a unique identifier, version number and date of implementation and reference to the previous version. The documents were prepared by/amended by the relevant personnel/reviewed by QMS Manager and Approved by the Director.

4. Records

DTLM had established and maintained procedures for the identification, collection, indexing, retrieval, storage, maintenance, and disposal of and access to quality and technical/scientific records. Original observations, including calculations and derived data, calibration, validation and verification records and final results were retained.

5. Data processing equipment

Electronic data was protected from unauthorized access and an audit trail was maintained. Computers and automated equipment were maintained to function properly. Electronic data was backed-up at regular intervals according to a documented procedure.

An inventory with ID no. of equipment and computerized systems was available with the information about software name and the section used.

6. Personnel

The laboratory had personnel with the necessary education, training, technical knowledge, and experience for their assigned functions.

SOP "Training of Staff Members" was checked. Four competency levels were identified.

Job description and training record of several persons were reviewed.

Training Schedule for 2022 was reviewed.

Job descriptions for all personnel involved in tests and/or calibrations, validations and verifications were maintained.

Headcount as per the company presentation was following:

Designation	No. of employees
Director	1
Technical Head	1
Deputy Drug Controllers	5
Pharmacist	13
Chemist	5
Microbiologist	1
Biomedical Engineer	1
Service Engineer	2
IT/Networking Supervisor	1
Computer Operator	1
Budget/Account Officer	1
Total	32

7. Premises

The laboratory facilities were of suitable size and design to suit the functions and to perform the operations to be conducted in them. Access to the laboratory was restricted to designated personnel (biometric access).

Control and monitoring of environmental conditions was explained in SOP "Procedure for Accommodation and Environment". Temperature and RH were monitored twice per day using Min/Max digital thermometers and recorded manually. This SOP also explained safety procedures. CCTV cameras were installed in all laboratories.

Separate storage facilities were maintained for the storage of samples, retained samples, reagents, laboratory accessories. All reagents including flammables were stored in one room. Inspectors were informed that in near future the Reagents Storage and Laboratory Accessories Storage will be moved to the new premises, which during inspection was under construction. Reagents, Laboratory Accessories and Documentation Archive were visited.

Reference standards were stored in separate room. T and RH were monitored.

Two diesel generators provided 100 kVA as emergency power-supply if the grid failed. The laboratory was also equipped with UPS systems to support the power-supply of laboratory's instruments and computerized systems.

8. Equipment, instrument, and other devices

Equipment, instruments, and other devices were designed, constructed, adapted, located, calibrated, qualified, verified and maintained as required by the operations to be carried out in the local environment. Volumetric glassware was uniquely labelled to ensure traceability.

9. Contracts

Outsourcing of testing was not permitted.

10. Reagents

Reagents and chemicals, including solvents and materials used in tests and assays were of appropriate quality. Reagents were purchased from approved suppliers and were accompanied by the Certificate of Analysis and the Material Safety Data Sheet.

Procurement of items, qualification of suppliers and externally provided services were explained in SOP "Procedure for Purchase of Supplies and Services". Evaluation, selection, monitoring of performance and re-evaluation of Service Providers was performed every 2 years. List of Service Providers and Approved Suppliers were presented.

Reagents and reagents prepared in laboratory were appropriately labelled.

A stock register was kept for all the reagents.

Purified Water was generated in the laboratory by RO Thermo Scientific equipment.

Tests were performed daily according to the USP Pharmacopoeia monograph for Purified Water.

Disposition of laboratory waste was explained in SOP "Disposition of Laboratory Waste". Disposition was contracted out. Waste sent out for disposal was recorded in Disposal and Incineration of Waste Control Log.

11. Reference substances and reference materials (CRS)

SOP "Standard Operating Procedure for Management of Reference Standards" explained receiving, recording, storage, distribution and disposing of certified reference standards. Upon receipt, CRS were verified against the specific Form. CRS were received from vendors and manufacturers and a limited number was purchased from the USP. Inspectors were informed that starting from 01/12/2022 all USP CRS will be purchased directly by DTLM.

Issuance of the CRS was recorded in "Working Standard Issuance Log Book".

After analysis, CRS were retrieved back from analysts and consumption and reconciliation was recorded in "CRS Inventory Log". Physical or chemical degradation, expired, broken or consumed status was recorded in CRS database. Certificates of Analysis were available for all CRS.

The register for all reference substances and reference materials was maintained in an Excel spreadsheet.

12. Calibration, verification of performance and qualification of equipment, instruments, and other devices

Each instrument was uniquely identified. Labels indicated the status of the calibration Equipment underwent DQ, IQ, OQ, and PQ, following a plan established by the laboratory. Balances were checked daily using internal calibration and using suitable test weights. Requalification was performed annually using certified reference weights.

Procedures were available for the qualification, handling, and maintenance of equipment used in the laboratory. Records/Log Books were kept for items of equipment. Usage of the instrument was recorded.

SOP "Standard Operating Procedure for the Management of Equipment". Calibration of laboratory equipment was contracted out. Calibration schedule was presented and cross-checked with implementation. Technical Manager and Biomedical Engineer was responsible for external calibration. Trend analysis was implemented in June 2021 and performed for all equipment calibrations.

Equipment preventive maintenance and calibration schedules were presented and cross-checked with implementation. PM was performed by Technical Manager and Biomedical Engineer following specific equipment PM forms.

13. Traceability

Traceability of the test reports to track the usage of reagents and equipment was ensured.
All calibrations or qualifications of instruments were traceable to certified reference materials.

14. Incoming samples

Samples were collected by Drug Inspectors and delivered to the laboratory. Only compliance samples were analyzed at DTLM.

SOP "Standard Operating Procedure for Receiving, Distribution, Handling of Test Items". The drug inspectors collected samples. Samples to the DTLM were delivered together with Form 6, which specified:

- Drug name
- Name of manufacturer
- Registration No.
- Batch No.
- Mfg. Date and Exp Date
- Quantity

The parcel barcode allocated at the time of sample receipt was scanned and the software generated unique sample identification number, which followed samples all the way till Certificate of Analysis.

Sample information was entered into the DTMS software.
Samples were divided in 3 parts for:

- Immediate testing
- Confirmation testing
- Retention

Immediate testing samples were distributed to the following sections:

- Dissolution
- Sterility
- Wet chemistry
- Physical-chemistry
- Retention
- HPLC

According to the Government Act, all tests should be performed in accordance with pharmacopoeias and or specifications. Tests items were distributed in accordance with Test Selection Matrix based on RA to define minimum quantity required for the test. Drug Inspectors had information about required sample amount for testing and minimum number of samples required for tests.

15. Analytical worksheet

Analytical workbooks were organized test wise and were issued by QSM, pages were numbered and bounded. Workbooks were separate for the different laboratory sections. DTLM practice was not to attach weighing slips to the Work Books, however it was noted that all meta data was traceable to the final report.

Good Chromatography Practices

Good chromatography practices were explained in SOP "Standard Operating Procedures for Good Chromatography Practices". Access and privileges were given to users according to their responsibilities.

Manual peak integration was not allowed, however eviewer was allowed to do manual integration after approval from Technical Head/Technical Manger on Inter office.

16. Validation and verification of analytical procedures

The laboratory did not perform any method validation.

SOP "Method Validation/Verification Protocol for HPLC" was checked. Method verification required the following to be performed:

- Linearity
- Specificity/Selectivity
- Intermediate precision

DTLM "Method Verification/Validation Plan" was available.

17. Testing

Compendial methods and manufacturers standard test procedures were used to allow analysts to perform the analysis in a reliable manner.

18. Evaluation of test results and OOS investigation

Out of specifications (OOS)

SOP "Out-Of-Specifications (OOS)" was in place, describing the conduct of investigations of OOS test results. SOP specified Phase Ia/Ib investigations and Phase II. Investigations were carried out according with the checklist.

If Analyst confirmed OOS, Government Analyst issued OOS investigation form and investigated the result along with QMS Manager & Reviewer. Where required, the investigation team was established to review audit trail and the whole process of testing.

SOP "Reporting of Results" explained procedure for checking of necessary documents attached with final report and a procedure for handling of Out-of-Specification (OOS) laboratory test results.

As per Drug Act 1976, the Government Analyst to whom a sample of any drug has been submitted for test and analysis by Provincial Drug Inspector, shall submit the signed report in quadruplicate in the prescribed form (Form-7 as per Punjab Drug Rules 2007) within sixty (60) days of the receipt by him of the sample of the drug. If he is not able to do so for the reasons beyond his control (such as standard, column, chemical, method, equipment or testing facility) shall communicate the reasons to the Inspectors in writing. If it is not possible to do so for the reasons beyond laboratory control (such as standard, column, chemical, method, equipment or testing facility) the reasons should be communicated to the Inspectors in writing with its copy to Provincial Quality Control Board. Provincial Quality Control Board shall have the sample tested from the same or any other Government Analyst or Government Drug Testing Laboratory or any other laboratory and PQCB (Board) will provide extension, if possible, for further period as may deemed possible by the Board.

Laboratory Supervisor was responsible to check all the steps and calculations performed by the Analyst, verify the data and sign the report.

According to the SOP, the Analyst attached the original weighing slip with the report. In case, when more than one sample had a single weighing slip then original weighing slips were attached with one report and copies with the others.

A Government Analyst forwarded to the Government a monthly report containing results of samples tested and analysed during the month for publication at the discretion of the Government.

Analyst submitted calculations, factors, tailing factor and audit trails to Government Analyst electronically on DTMS. After submission, results appeared on the dashboard (DTMS) of Government Analyst. The Government Analyst submitted the report and Form-7. Total of four Original copies of Form-7 were generated; two copies to sample sending authority and one copy each for the record of Pakistani Quality Control Board and DTL. After printing of Form-7, Government Analyst signed and stamped the report and forwarded it to Dispatch Officer who attached signed forwarding letter and dispatch it to concerned authorities. Forwarding letter was signed by a Director or any other person authorized by the Director.

A statement of conformity to a specification was provided by the Government Analyst on the Form -7 which states "In the opinion of the undersigned, the sample referred to above is of Standard Quality as defined in Drug Act 1976 and rules thereunder.

19. Certificate of analysis

Certificate of Analysis was prepared for each analysis.

20. Retained samples

Retained samples were kept in their final pack and retained as required by the legislation, i.e., one year after expiry date.

21. Safety

Staff wore laboratory coats. Goggles were provided. Safety showers were installed. Material Safety Data Sheets were available.

Part 3 - Conclusion

Based on the areas inspected, the people met and the documents reviewed, including the CAPA plan provided for the observations listed in the Inspection Report, ***Drugs Testing Laboratory Punjab, Multan (DTLM),*** *located at* ***Near Kidney Center, Muzaffar Ghar Road, Multan, Punjab, Pakistan*** was considered to be operating with WHO Good Practices for Pharmaceutical Quality Control Laboratories 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 Laboratory, 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 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 GPPQCL Guidelines or ***TRS No. 957, Annex 1***
   https://www.who.int/publications/m/item/who-good-practices-for-pharmaceutical-quality-control-laboratories---trs-957---annex-1

2. 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

3. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3.
   Short name: WHO TRS No. 1033, Annex 3
   9789240020900-eng.pdf (who.int)

4. 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

5. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4.
   Short name: WHO TRS No. 1033, Annex 4
   https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations

6. 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 GMP guidelines or ***TRS No. 986, Annex 2***
   https://apps.who.int/iris/bitstream/handle/10665/112733/WHO_TRS_986_eng.pdf?sequence=1

7. 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://apps.who.int/iris/bitstream/handle/10665/44291/WHO_TRS_957_eng.pdf?sequence=1

8. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3.
   Short name: WHO TRS No. 957, Annex 3
   https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/production/trs957-annex3-gmp-pharmaceutical-products-containing-hazardous-substances.pdf?sfvrsn=bd8e1374_5&download=true

9. WHO good manufacturing practices for sterile 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 6.
   Short name: WHO TRS No. 961, Annex 6
   http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

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

11. 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

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 (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

13. 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 (WHO Technical Report Series, No. 1010), Annex 8.
    Short name: WHO TRS No. 1010, Annex 8
    https://www.who.int/docs/default-source/medicines/norms-and-standards/guidelines/production/trs1010-annex8-who-gmp-heating-ventilation-airconditioning.pdf?sfvrsn=c77698e2_0

14. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-third Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1019), Annex 2. **Short name: WHO TRS No. 1019, Annex 2**
https://digicollections.net/medicinedocs/documents/s23699en/s23699en.pdf

15. 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
https://www.who.int/docs/default-source/medicines/norms-and-standards/guidelines/production/trs981-annex2-who-quality-risk-management.pdf

16. 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
https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/prequalification/trs981-annex3-who-variations-prequalified-product.pdf?sfvrsn=809e81b_2

17. WHO guidelines for preparing a laboratory information file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 13.
Short name: WHO TRS No. 961, Annex 13
https://www.who.int/docs/default-source/medicines/norms-and-standards/guidelines/quality-control/trs961-annex13-guidelines-preparing-laboratory-information-file.pdf?sfvrsn=54d1f397_2

18. Good Manufacturing Practices: Guidelines on validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3. ***Short name: WHO TRS No. 1019, Annex 3***
https://digicollections.net/medicinedocs/documents/s23697en/s23697en.pdf

19. 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***
https://www.who.int/publications/i/item/9789241209922

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 (WHO Technical Report Series, No. 992), Annex 5. ***Short name: WHO TRS No. 992, Annex 5***
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