World Health Organization

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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
of the Quality Control laboratory

Part 1	**General information**
Laboratory Details	
Name of the laboratory	Drugs Testing Laboratory (DTL) Punjab, Lahore Primary and Secondary Healthcare Department Government of Punjab
Address of inspected laboratory	1 - Birdwood Road Lahore-54000 Pakistan
GPS Coordinates	Latitude: 31.5489061 Longitude: 74.3240123
Address of corporate office, telephone number and fax number	Same as above
Dates of inspection	12 - 14 December 2022
Type of inspection	Initial
Introduction	
Brief description of testing activities	

Type of analysis	**Finished products**	**Active pharmaceutical ingredients**
Physical/ Chemical analysis	pH, Water content by KF, Loss on drying, Friability, Tablet hardness, Tablet dimensions, Uniformity of dosage units (mass, content), Disintegration time, Dissolution, Density/Specific gravity, Conductivity, Particulate matter, Deliverable volume, Extractable volume	pH, Water content, Loss on drying, Density, Conductivity, Refractive index, Optical rotation
Identification	FTIR, TLC, HPLC (UV-VIS, DAD, RI, FLR, ECD detection), UHPLC (UV-VIS, DAD, RI, FLR, MS detection), UPLC (UV-	FTIR, TLC, HPLC (UV-VIS, DAD, RI, FLR, ECD detection), UHPLC (UV-VIS, DAD, RI, FLR, MS detection), UPLC (UV-

		VIS, DAD detection), GC-MS, GC-FID AAS, Flame photometry, UV-VIS spectrophotometry, and basic tests	VIS, DAD detection), GC-MS, GC-FID AAS, Flame photometry, UVVIS spectrophotometry, and basic tests
	Assay, impurities, and related substances	HPLC (UV-VIS, DAD, RI, FLR, ECD detection), UHPLC (UV-VIS, DAD, RI, FLR, MS detection), UPLC (UV-VIS, DAD, MS detection), GC-MS/FID, AAS, FTIR, Flame photometry, UV-VIS spectrophotometry, Volumetric titration, Polarimetry, Refractometry, Potentiometric titration	HPLC (UV-VIS, DAD, RI, FLR, MS, ECD detection), UHPLC (UV-VIS, DAD, RI, FLR, MS, ECD detection), UPLC (UV-VIS, DAD, MS detection), GC (MS/FID), AAS, FTIR, flame photometry, UV-VIS spectrophotometry, Volumetric titrations, Polarimetry, Refractometry, Potentiometric titration
General information	The Drugs Testing Laboratory Punjab Lahore, commonly known as DTL Lahore, is a Regulatory Laboratory working under the Primary & Secondary Healthcare Department, Government of the Punjab. It was established in 1970 and later came under Drugs Act 1976. The Drugs Testing Laboratory Punjab, Lahore is now governed by Drugs Act 1976 and The Punjab Drugs Rules 2007. A major upgrade and restructuring of DTL Lahore was carried out at the start of 2016 when the old premises was revamped into a new laboratory. The Drugs Testing Laboratory Lahore was inaugurated in February 2016, which has been accredited on ISO/IEC 17025 by Pakistan National Accreditation Council (PNAC) in August 2018. The Drugs Testing Laboratory Punjab, Lahore was a provider of analytical services only.		
History	This was the first inspection carried out by WHO Prequalification team. The Drugs Testing Laboratory Lahore has been accredited by Pakistan National Accreditation Council on ISO/IEC 17025 - The Laboratory Accreditation Certificate Number is LAB: 162.		
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
CS	Computerized system
CoA	Certificate of analysis
CAPA	Corrective action and Preventive action
DQ	Design qualification
DRAP	Drugs Regulatory Authority of Pakistan
FPP	Finished pharmaceutical product
FTIR	Fourier transform infrared spectrophotometry or spectrophotometer
GC	Gas chromatography or Gas chromatography equipment
GMP	Good manufacturing practices
HPLC	High-performance liquid chromatography (or high-performance liquid chromatography equipment)
IQ	Installation qualification
IR	Infrared spectrophotometry
ISO	International Standards Organization
KF	Karl Fischer 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
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 Lahore (DTL) was legally authorized to function and can be held legally responsible. DTL 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. DTL had in place organizational charts, detailing the organization and management structure of the laboratory.

2. Quality management system

The management system was explained in the following documents:

- Quality Manual (QM), Policies
- Quality Procedures (SOPs)
- Work Instructions, Analytical Procedures
- Quality Forms (Controlled Formats), Log Books, Labels

DTL 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 DTL were periodically audited internally and externally. Management review of quality issues were regularly undertaken.

DTL participated in Proficiency Testing schemes every year for HPLC analysis, pH testing, Conductivity, Sterility testing, GC analysis, endotoxin testing, Atomic absorption analysis, Disintegration test, Dissolution analysis, Water content determination (KF), FTIR analysis, Refractive index measurement, Friability testing, Weight variation, Hardness testing, Tablet dimensions, UV spectrophotometric analysis and Titrimetric analysis with different PT providers.

DTL conducted retesting of retained portion of the analyzed samples within the laboratory at intervals for Performance Evaluation.

DTL participated in inter-laboratory comparison activity with different Laboratories for different parameters i.e., HPLC, UV, Weight variation, Extractable volume, Flame photometry, Atomic absorption, Water by KF, FTIR, Polarimetric analysis, Endotoxin, Sterility testing, Disintegration, Dissolution test.

The following policies were in place:

- Policy for Computer System Administration. Password policy.
- Access Authorization and Security Policy - Biometric control system was installed for access to laboratory premises, CCTV cameras were installed in all laboratories and corridors.
- Policy for Confidentiality and Conflict of Interests.

Management review (MRM)

SOP "Quality Management System" explained procedure and level by which management reviews were performed. According to the SOP, a review of the quality management system was performed at least annually. Standard agenda was specified. Findings from management reviews and the actions that arose from MRM were recorded. Last MRM meeting minutes and attendance record were presented to inspectors and discussed.

Data integrity

SOP "Procedure for the Data Integrity and Data Traceability" explained data integrity and data traceability and ALCOA+ principles of paper records and electronic records.

Electronic data: batch sequence for each analysis, audit trail and processing method parameters were discussed.

Report for computerized system validation of chromatographic data system with Empower software specified seven (7) access levels.

SOP "Disaster Recovery Management" explained procedures for disaster recovery in case of facility disaster, network disaster, hardware disaster, software disaster and data disaster.

SOP "Procedure for Backup, Restoration, Storage of Electronic Data" was applicable to all computer-generated data. Back up Log Book was presented.

CDS system was used for the centralized management of chromatographic data. All chromatographic systems used for routine analysis were connected to the server and operated through Empower software.

Computer system validation was performed. Protocol for Computerized System Validation (CVA) of Chromatographic Data System was discussed. Computer system validation/verification plan for year 2022 - 2023 was presented.

Change control (CC)
Change management was performed in accordance with SOP "Change Control Management System". All the changes that may affect the quality of analysis and good laboratory practice were controlled through the change control management system.

A number of Change Controls records were discussed.

Handling of non-conformances (deviations)
Handling of non-conformances were described in two (2) SOPs, namely SOP "Procedure for Deviation Handling" and "Standard Operating Procedure for the Control of Non-conforming Work Reporting of Anomalies".

SOP "Procedure for Deviation Handling" was applicable to all the sections responsible for carrying out activities which may impact the validity of results or quality of the analytical work performed at DTL.

Deviations were classified as:
- Critical
- Major
- Minor

Deviations could be:
- Planned
- Unplanned

A number of deviation records were discussed.

SOP "Standard Operating Procedure for the Control of Non-conforming Work Reporting of Anomalies" specified anomaly/non-conforming work possible cases.

The significance of the anomaly/non-conforming work was classified as:
- Highly significant
- Significant
- Non-significant

A number of Anomalies Logs were discussed.

Corrective actions (CA)
SOP "Standard Operating Procedure for the Corrective Action (CA)" indicated different source documents of CA. Four (4) steps for CA were specified.

A number of Corrective Action Logs were discussed.

Complaints
Handling of complaints was described in SOP "Procedure for Receiving, Analyzing, Improving, Reviewing and Maintaining Records of Customer Feedback and Customer Complaints". SOP was applicable to customer feedback and customer complaints relating to the laboratory activities i.e., quality of the analysis, operation, and management system. Complaints closing time was specified. Customer feedback was requested from the external customers on annual basis. Complaints were trended, trends were presented.

A number of complaint records were discussed.

Risk Management system
Risk assessment was described in "SOP for Quality Risk Management". Quality risk assessments was recorded on "Risk Assessment Form" and the summary of action was recorded on "Risk Assessment Summary Form".

Internal audits
SOP "Standard Operating Procedure for the Internal Audit" addressed all elements of the ISO/IEC 17025.

The activities of DTL Lahore were systematically audited to verify compliance with the requirements of the Quality Management System (QMS). The internal audits were carried out by trained and qualified personnel. The QMS Manager was responsible for planning and organizing the internal audit.

Observations were classified as:
- Critical
- Major
- Minor
- Suggestions

Internal audit schedule for 2022 was presented and well as last Internal Audit Report. Checklists were used to perform audits.

External audits
List of external audits carried out from 2019 was presented.

3. Control of documentation

DTL 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 of documents was established and was readily available.

Documents had a unique identifier, revision number and date of implementation and reference to the previous version.

Relevant staff was trained on new and revised SOPs; the personnel acknowledged by signature that they were aware of applicable changes.

4. Records

DTL had established and maintained procedures for the identification, collection, indexing, retrieval, storage, maintenance, and disposal of and access to all quality and technical/scientific records. Original observations, including calculations and derived data, calibration, validation and verification records and final results were retained for 5 years. OOS related document files were retained without time limitation.

5. Data processing equipment

Procedures were established and implemented for protecting the integrity of data. Electronic data was protected from unauthorized access and an audit trail of any amendments was maintained. Computers and automated equipment were maintained to function properly.

An inventory, of all computerized systems was available.

6. Personnel

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

Headcount as per the company presentation:

Director	1
Director Technical	2
Deputy Drugs Controller	5
Pharmacologist	1
QMS Manager	1
Pharmacist/Analyst	53
Senior Microbiologist	1
Assistant Bacteriologist	1
Microbiologist	1
Biochemist	2
Analytical Chemist	17
Budget and Accounts Officer	2
Data Processing Officer	1
Networking Supervisor	1
Biomedical Engineer	3
Computer Operator	4
Total	96
Current complement	74

SOP “Training Program in Drug Testing Laboratory (DTL) Lahore” defined the DTL internal training program to ensure the competency of laboratory personnel. According to the SOP, there were three (3) competency levels.

Form “Orientation Schedule” and Form “Skill Matrix for the Quality Management System” was in place.

Personnel undergoing training was assessed on completion of the training. The laboratory maintained the records for technical personnel.

Training on Good Documentation practices as well as a number of staff training records were discussed.

Current job descriptions for all personnel involved in testing and/or calibrations, validations and verifications were maintained.

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. A layout of the premises was available. Access to the laboratory and storage facilities was restricted to designated personnel and controlled by biometric access system. The laboratories and corridors were monitored using a CCTV system.

Separate storage facilities were maintained for the storage of retained samples, reagents, gases and laboratory accessories, and reference substances. Compressed gases used for GC analysis were stored chained in locked metal cabinet.

Two diesel generators provided 200 kVA and 500 kVA as emergency power-supply if the grid failed.. The laboratory was also equipped with 33 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. Labels attached to the equipment had a unique identification label and calibration status label.

9. Contracts

Outsourcing of testing was not permitted as per The Drugs Act 1976 and DRAP Act 2012.
A number of contracts were discussed.

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 reagents was explained in SOP "Standard Operating Procedure for Procurement". Procurement was done following PPRA (Public Procurement Regulatory Authority) Rule 2014.

SOP "Standard Operating Procedure for Inventory Receiving and Issuance" explained inventory issuance at Drug Testing Laboratory, Lahore following the applicable legislation i.e., PPRA Rule 2014. Physical inspection of the received items was performed according to the "Physical Inspection Checklist.

Reagents stock was maintained as an Excel sheet.

Vendor/supplier verification procedure was explained in SOP "Standard Operating Procedure for Supplier Qualification". It applied to chemicals, equipment, equipment parts, glassware, analytical accessories, calibration, maintenance etc. DTL was adhering to Public Procurement Regulatory Authority (PPRA) Rule 2014.Vendor evaluation criteria was specified.

Reagents prepared in laboratory were appropriately labelled.

Labels of purchased reagents specified:
- Content
- Manufacturer
- Date received and date of opening of the container
- Storage conditions
- Expiry date or retest date

Purified water (PW) generated by RO system was used for analysis, preparation of reagents and final rinsing of glassware. Conductivity was checked and recorded daily.

11. Reference substances and reference materials

SOP "Procedure for Receiving, Storage, Utilization and Management of Primary/Secondary/Standardized Working/Manufacturer Working Standards" explained procedure for the receiving, storage, issuance, utilization, and management of standards. Reference standards were managed by Reference Standards Section. Reference standards were stored in accordance with storage conditions, T and RH were monitored.

The register for all reference substances and reference materials was maintained.

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

Instruments were uniquely identified. Labels indicated the status of the calibration and the date when recalibration was due.

SOP "Standard Operating Procedure for the Qualification of Equipment, Facility, Utility and System" was applicable to all the equipment, facility, utility and/or system. Equipment qualification schedule was available, Validation/Verification Plan "Qualification of Equipment" for 2023 was presented.

Qualification of a number of equipment was discussed.

SOP "Standard Operating Procedure for Preventive Maintenance" explained equipment PM procedure. Annual Preventive Maintenance calendar year 2022 presented and checked. PM was performed quarterly, for some equipment PM was performed monthly. PM was performed in accordance with equipment specific checklists. PM of a number of equipment was discussed. Separate Log Books were used for different apparatus performance verification records.

13. Traceability

Traceability of the test reports to track the usage of reagents and equipment was ensured.

14. Incoming samples

Samples were collected by the drug inspectors and delivered to the DTL along with "Memorandum to Government Analyst: Form-6".

Samples were received in accordance with the Drugs Act 1976/DRAP Act 2012, the Punjab Drugs Rules 2007, and their amendments.

A "Form-6", accompanied each sample submitted to the laboratory, and contained the following information:

- Name of drug
- Name of manufacturer
- Registration No.
- Batch No.
- Manufacturing Date
- Expiry Date
- Quantity
- Physical condition of sample
- Stamp of Drug Inspector/Government Institution
- Physical inspection Performa (For Hospital samples)
- Storage condition
- Applicable fee in cash/Challan Form 32-A

SOP "Standard Operating Procedure for Receiving of Sample in Drug Testing Laboratory Lahore" was discussed.

Samples were received, reviewed, and registered by Sample Receiving Officer in DTMS software.

SOP "Standard Operating Procedure for Distribution of Sample in Drug Testing Laboratory Punjab, Lahore" was discussed. Samples were distributed by Sample Receiving Officer (SRO). Barcode stickers were placed on the sample portions according to analysis. The divided portions of the samples were placed in respective laboratory basket or respective rack in refrigerator.

Samples were divided in two parts: Immediate testing and retention samples. If samples were required for confirmation of testing, these were withdrawn from retention samples.

Visual inspection of samples was carried out by SRO upon receipt.

15. Analytical worksheet (Work Book)

In DTL, analytical raw data was recorded in individual Analyst Work Books. Work Books were dedicated to analysts and laboratories. Work books contained required information. Different laboratory Work Books had different analyst Work Sheets related to specific tests. Work Sheets were traceable to equipment, reagents/mobile phases, and reference standards. Work Sheets were issued by QMS department.

Excel spreadsheets were used for different calculations. Excel sheet validation was performed. Report for Excel Spreadsheet Validation for Calculations of Weight Variations for Capsules and calculation of Assay verification by HPLC was checked as an example. Validation/verification plan for 2023 for Excel spreadsheets was presented.

16. Validation & verification of analytical procedures

The laboratory did not perform any method validations.

SOP "Procedure for the Analytical Method Validation/Verification" was discussed.
Method Verification Protocol for an ID and Assay HPLC method was discussed.

17. Testing

Compendial methods and manufacturers specifications were used as test procedures. Current pharmacopeias and manufacturers specifications were available. Manufacturer's specifications were distributed to analysts upon request by Reference standard laboratory.

SOP "Standard Operating Procedure for the System Suitability (SS), Quality Check Standard and Sample Analysis on HPLC and UV" explained SS tests criteria and injection sequence.

SOP "Standard Operating Procedure for the Chromatographic Column Management" explained the procedure to ensure the identification, issuance, utilization, retrieval, maintenance, disposal of and record keeping of chromatographic columns. Each column used at DTL was assigned a unique column identification number. "Log Book for Column Maintenance & Utilization Record" had a separate page for the different columns. Columns were stored in original packaging.

<u>Evaluation of test results and Out of Specification investigation</u>
Test results were reviewed and evaluated.

SOP "Standard Operating Procedure for Reporting of Samples in Drug Testing Laboratory Punjab, Lahore" explained reporting procedure by checking necessary documents attached with final report.

Internal analytical report form (separate for different laboratories) contained test description, specification or limits, method of analysis, results. Form was signed by analyst, reviewed, and signed by reviewer and submitted to Government Analyst. Raw data was copied and attached to the internal report.

Analytical Work Books were separate for different laboratories. Analysts and reviewer signed each page of book. Reviewer checked results and calculations and audit trails were applicable.

Out of Specification (OOS)
OOS investigation procedure was explained in "Standard Operating Procedure for Handling and Reporting of OOS results". When an OOS results was obtained, a laboratory investigation was initiated using the "Preliminary Laboratory Investigation Report".

SOP and flow diagram explained:
- Phase I Investigation
- Phase-II Investigation

Activities related to OOS investigations were supervised by Governmental Analyst.

OOS Investigation File for Paracetamol assay was checked.

18. Certificate of analysis

Certificate of Analysis was prepared for each analysis. CoA was prepared/signed by Government Analyst, reviewed/signed by Deputy QMS Manager and approved/signed by QMS Manager.

19. Retained samples

Retained samples were kept in their final pack and retained Pass Samples will be retained for 90 days from the issuance of the report on Form-7, Failed samples (No Litigation Reported) will be retained for180 days from the issuance of the report on Form-7 and Failed Sample (Under Litigation) will be retained till the days after the receipt of the decision in writing from the respective court/applet board and/or PQCB, these samples will be retained for 60days as required by the legislation, i.e., one year after expiry date.

20. Safety

Staff was wearing laboratory coats. Goggles were provided. Safety showers were installed. Rubber suction bulbs were used on manual pipettes. 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, ***Government of Punjab, Primary and Secondary Healthcare Department, Drug Testing Laboratory (DTL), located at 1 - Birdwood Road, Lahore-54000, 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***
https://www.who.int/publications/i/item/9789241209922

21. Production of water for injection by means other than distillation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 3. ***Short name: WHO TRS No. 1025, Annex 3***
https://www.who.int/publications-detail/978-92-4-000182-4

22. 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 (WHO Technical Report Series, No. 1010), Annex 10.
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