World Health Organization

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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Quality Control Laboratory

Part 1	**General information**		
Inspected laboratory details			
Name of laboratory	Mission for Essential Drugs and Supplies (MEDS)		
Address of inspected laboratory	Mombasa Road, opposite Nation Printing Press P.O. Box 78040 Viwandani, 00507 Nairobi, Kenya		
GPS Coordinates	Latitude: -1.3649 Longitude: 36.9080		
Inspection details			
Dates of inspection	15-16 April 2019		
Type of inspection	Follow-up		
Introduction			
Brief description of testing activities	*Type of analysis*	*Finished products*	*Active pharmaceutical ingredients*
	Physical/ Chemical analysis	pH, loss on drying, water content, refractometry, friability, disintegration, dissolution, density, uniformity of dosage unit (mass, content)	pH, loss on drying, water content, refractometry, density
	Identification	HPLC (UV-VIS, DAD, RID, fluorescence detection), GC, UV-VIS and IR spectrophotometry, TLC, chemical reaction	HPLC (UV-VIS, DAD, RID, fluorescence detection), GC, UV-VIS and IR spectrophotometry, TLC, chemical reaction
	Assay, impurities and related substances	HPLC (UV-VIS, DAD, RID, fluorescence detection), UV-VIS spectrophotometry, GC, volumetric titrations, polarimetry, Determination of related substances/impurities	HPLC (UV-VIS, DAD, RID, fluorescence detection), UV-VIS spectrophotometry, GC, volumetric titrations, polarimetry, Determination of related substances/impurities

		and degradation products	and degradation products
	Micro-biological tests	Bacterial endotoxins test (LAL) – Kinetic Chromogenic Method	Bacterial endotoxins test (LAL) – Kinetic Chromogenic Method

General information	MEDS is a Christian non-profit organization, located in Nairobi, Kenya. The organization was founded in 1986 and is registered as an ecumenical partnership for improving access to quality healthcare through provision of essential medicines, medical supplies and capacity building. MEDS Quality Control Laboratory (QCL) started its operations in 1997. MEDS QCL performs QC testing of Finished Pharmaceutical Products and Active Pharmaceutical Ingredients for Pharmaceutical Procurement Agencies, Pharmaceutical Manufacturers and Distributors, Regulatory Bodies and Donor Funded Programs.
History	The QCL was pre-qualified by WHO in March 2009 and continued to comply with WHO standards after inspections in August 2012, June 2015 and August 2018. Last ISO 9001:2015 certification audit was held in September 2017, which included the laboratory services provided by the QCL.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	This inspection was a follow up of the previous inspection held in August 2018. Nevertheless, the scope of inspection also included a review of the other laboratory activities including: - Organization and management - Quality Management - Data processing - Premises - Evaluation of test results, including investigation of OOS - Personnel – Training - Equipment – Calibration – Performance check - Traceability - Sample and material management - Supplier and contractors - Safety
Restrictions	Following last WHO Inspection held in August 2018, Bacterial endotoxins test (LAL) – Kinetic Chromogenic Method was transferred to the service provider Analabs Limited.

Out of Scope	The organization did not have a section to perform pharmaceutical microbiology laboratory activities.
Abbreviations	**Meaning**
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
CoA	Certificate of analysis
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)
KF	Karl Fisher titration
LIMS	Laboratory information management system
MB	Microbiology
MR	Management review
NC	Non-conformity
NCA	National control authority
NCL	National control laboratory
NRA	National regulatory agency
OOS	Out-of-specifications test result
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
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometry or spectrophotometer

Part 2	Summary of findings and recommendations

1. Organization and management

The laboratory operated as part of MEDS, which is legally registered. MEDS Senior Management supported a high level of Quality Assurance in the company.

MEDS had defined the organization and management structure of the organization, including the quality control laboratory, responsibilities, authority and interrelationship of the personnel in the organogram. The Laboratory Supervisor was reporting directly to the Quality Assurance Manager, who was also responsible for issuing and signing off the CoAs. MEDS's organizational chart was under revision to define the current management structure (including a new unit for Quality Services) and the relationships between management, technical operations and support services. The total number of staff in the laboratory accounted 22 at the time of inspection. The laboratory was supervised by Mrs. Mildred Wanyama.

The organization had arrangements to ensure that its management and personnel were not subjected to commercial, political, financial and other pressures or conflicts of interest that might adversely affect the quality of their work, and that they had appropriate authority and resources needed to carry out their duties as defined in their job descriptions. There was a policy in place to ensure confidentiality of information contained in marketing authorizations, transfer of results and reports and to protect data in archives (paper and electronic form).

The deficiencies identified during the inspection were adequately addressed in the provided CAPA plan.

2. Quality management system

A quality manual defining the quality management system and addressing all company activities was available. For each area defined in MEDS QM, a specific SOP was available. The QMS consisted of Quality Manual, Quality Policy & Quality Objectives, organizational structure, procedures and work instructions to ensure the quality of all activities carried out within the organization.

The list of valid SOPs was provided. The list contained 240 SOPs divided in 10 groups, where 84 were exclusively dedicated to the laboratory activities.

Proficiency testing

The laboratory participated in proficiency testing schemes on a regular basis, arranged by WHO, EDQM and MUHAS (Pharm R&D Lab, School of Pharmacy, Muhimbili University of Health and Allied Sciences, Tanzania). A list of all participations, and respective results, from 2012 until 2018 was provided. Last participation in proficiency testing was recorded on November 2018, performing the assay of metronidazole in tablets (MUHAS), with satisfactory results. Two more participations were expected to be carried out in 2019, arranged by WHO (EQAAS Phase 9) and by MUHAS (assay and dissolution of co-trimoxazole tablets).

Internal audits

The activities of the laboratory were systematically and periodically audited internally in accordance with the applicable SOP. The related CAPA was handled as per the respective SOP.

List of service providers for 2018/2019 was available, divided in

- Supplier of consumables
- Technical service providers

Suppliers were audited in accordance with a Working Instruction. The organization had a process to publish an advertisement on a daily newspaper to request for new applications on services they needed to be provided. Both current and new service providers would be invited to apply for the tender. A new assessment of all applicants, as well as an audit on the shortlisted selection would take place to enable the final decision in accordance with SOP for supplier selection.

Management Review

Management reviews were performed quarterly in accordance with the respective SOP, covering audit reports, complaints, and non-conforming work. The agenda and the minutes of the meeting of the last management review, arranged on 25 Jan 2019 were reviewed.

Change control

SOP for Change control management and relating template was reviewed.

Management of Deviations

The applicable SOPs and process were reviewed.

Corrective Action and Preventive Action

Identification, investigation, correction, approval and closure of quality events, as well as trending of CAPAs were carried out in accordance with the applicable SOP. The laboratory had started to record and classify CAPAs in a logbook since February 2019.

Risk management

The applicable SOP was reviewed. The procedure applied to risk assessment, risk control, risk communication and risk review in MEDS quality management system, including data integrity, changes to process and specific equipment, technology, regulatory requirement and safety. A risk register template was provided to identify about 30 risks related to the abovementioned areas. The likelihood of occurrence, risk evaluation, risk mitigation and other relevant activities were identified with the aid of a scoring system.

The deficiencies identified in relation to the quality management were properly addressed.

3. Control of documentation

A system of procedures was established and maintained to control all documents (preparation, revision, distribution, return, archiving) in accordance with SOPs for control of documented information, and for control of retained documented information. A master list identifying the current version status and distribution of documents was available. Revision of SOPs was monitored and managed by Quality Management using a template for "Technical documented information change notice".

The SOPs were uploaded in and managed by an electronic system incorporated in the MEDS Intranet, with restricted access control. The entire staff had the read-access to the valid SOPs. The original SOPs were kept in paper format. All SOPs were reviewed every two years for relevance and applicability. The system was adequately demonstrated by IT-staff.

The relevant staff were trained on new and revised SOPs.

The deficiencies identified on the control of documentation were properly addressed in the provided CAPA plan.

4. Records

Record of analytical tests were documented, including calculation and derived data, method validations/ verifications, instrument use, calibrations and maintenance and sample receipt in log books containing consecutively numbered pages. The records were complete and signed, alterations were commented, and references were made to appendices containing the relevant recordings, e.g. chromatograms and spectra. The applicable specifications were consistently used with the information currently held in the manufacturer documentation or in the pharmacopoeial references. These operations were described in the respective SOP.

The deficiencies identified on records were adequately improved.

5. Data processing equipment

An inventory list of all computerized systems was available. The records on hardware configuration, installation and changes (incl. software updates) were kept for computerized systems which were components of test equipment.

Implementation of Labware LIMS software for management of laboratory information was in process to meet the various needs of the laboratory.

Windows XP operating systems were either upgraded or retired.

Instruments such as HPLCs, UV-Vis and IR were linked to the computers operated by their respective software systems. All raw data generated were stored as hard copies, as well as electronically on a server. SOP for Sample Analysis described how the laboratory established and maintained instructions to ensure that the integrity of data generated by data processing equipment was protected.

OpenLab Ezchrom software system was a chromatography database linked to the HPLC equipment. The qualification documentation of the equipment and the software system was provided. The URS document was replaced by the justification document of the purchase of Ezchrom software for HPLC. Installation qualification (IQ), operational qualification and performance verification (OQPV) of the equipment were carried out by the vendor and approved by the laboratory supervisor. Correspondingly, the IQ and PQ documentation of Ezchrom software system were provided. The access rights privileges and the proof of fully protected audit trail of the software system were verified.

It was recently required to provide a technical agreement for purchase of any software system to replace the URS documentation.

SOP for Access control to HPLC software systems was reviewed. The usage of equipment was recorded in the respective logbook.

Computer generated, time-stamped audit trails for electronic records were generally maintained for a number of computerized systems.

Electronic data was backed up at regular intervals. Incremental backup was also automatically provided by running SQL script. The backed-up data were stored in the cloud system offered by the facility's internet provider. The assessment of service provider was carried out in accordance with the applicable procedure. Regular backups were stored on hard-drive systems, protected in the server room located in the G-floor, and only accessed by ICT.

Restoration of data was carried out to ensure that backup data were exact and complete through their life-cycle and that they were secure against alteration, inadvertent erasures or loss. Data restoration was required to be carried out in the end of each month and recorded on a template for "SYSPRO data restore" where information about date of restoration, server IP address and respective verification was described.

SOP for Validation Master plan for computerized systems, together with a list of computerized software systems were available.

Spreadsheets (e.g. Excel®), were designed by the IT-staff. All cells including calculations were locked so that formulas could not accidentally overwritten. Free access was only given to cells to be filled in with data. Spreadsheets were stored on the server where the analyst had access to with specific username and password. Excel spreadsheets were validated and properly managed.

The deficiencies identified on the data processing were addressed in the provided CAPA plan.

6. Personnel

Training of personnel was managed through SOP for Human Resources Development procedure. Personnel Internal Training programme for 2017, 2018 and 2019, as well as Internal Qualification Programme for 2019 were reviewed.

The laboratory had generally sufficient personnel with the necessary education, training, technical knowledge and experiences for their assigned functions. Staff undergoing training were assessed on completion of the training, using the Laboratory Personnel Training evaluation form.

Regarding the training of new laboratory staff, a specific training program was developed for each new member of the team.

Randomly selected training Program and related training documentation for the new Lab Assistant and new Lab Analyst were confirmed.

Job descriptions were maintained for all laboratory personnel, including those involved in tests and/or calibrations, validations and verification activities. Records were also maintained of all technical personnel describing their qualifications, training and experience.

The deficiencies identified on the personnel were properly addressed.

7. Premises

The laboratory facilities were of suitable size, design, construction and location. The facilities were clean, tidy and well organized, demonstrating to be suitable for the laboratory activities.

Separate storage facilities were maintained for the secure storage of samples, retained samples, reagents, laboratory accessories and reference substances, if necessary under refrigeration (2-8°C) and frozen (-20°C). The environmental conditions of these rooms were monitored and controlled.

The laboratory had two rooms in which LAL testing – Kinetic Chromogenic Method - could be performed. This specific test did not require the same environmental conditions as required for sterility testing. These two rooms were self-contained, and could be fully dedicated to the LAL testing, provided that any possibility of cross-contamination was minimized. Quality control parameters, as well as system suitability parameters were implemented, in order to demonstrate that there were no external interferences in the test procedure, in accordance with the specific pharmacopoeial chapters for Bacterial Endotoxins.

The access to the laboratory facilities was restricted to designated personnel. Dedicated area for storage of flammables and hazardous material were available.

The deficiencies identified on the premises were adequately addressed.

8. Equipment, instrument and other devices

The equipment, instruments and other devices used for the performance of tests, calibrations, validations and verifications were inspected to verify whether they met the applicable requirements. The required test equipment and instruments for the performance of laboratory activities, including preparation of samples and the processing of and analysis of test and/or calibration of data were available.

The following equipment were randomly selected to verify the adequacy of their calibration/validation certificates:

- pH meter
- Calibrated Temperature probe
- HPLC column
- Dissolution tester
- Calibrated tachometer
- FTIR
- HPLC Instrument
- Balance room, balances in use and a randomly selected calibration certificate, together with the calibration certification of the weights used for daily performance verification.

- Titrator
- HPLC Shimadzu
- HPLC EQ-078 was out of order. OQR was carried out on 4 Apr 2019 and the service report was pending. The records were properly documented.
- Installation documentation, user manual and calibration certification of disintegration apparatus, together with the calibration certificate of temperature probe and the stop watch

The deficiencies identified on the equipment were addressed in the provided CAPA plan.

9. Contracts

The laboratory had a procedure in place for the selection and purchasing of services and supplies. For details refer to section 2 of this report.

Contracts were signed and defined the contracted work and established duties and responsibilities for each party. The competence of the contracted organizations was assessed, and records of these assessments were kept accordingly.

The contract of analytical services for sterility testing, bioburden testing, extraction and bacterial enumeration test, microbial assay and efficacy tests for disinfectants with the respective laboratory was reviewed. A modified contract to include the use of facility for BET test performance was implemented on 11 Feb 2019.

The deficiencies identified on the contract were adequately addressed.

10. Reagents

Reagents and other materials were purchased centrally. The reagents used were of appropriate quality and correctly labelled. Labels of reagents contained the required information.

Reagent solutions prepared in the laboratory were labelled with the name of the reagent, date of preparations and initials of technician or analyst, expiry date or retest date, as justified and concentration, if applicable.

Reagents inventory list, as well as a template for each reagent to record the consumption of reagents were available.

The deficiencies identified on the reagents were adequately addressed.

11. Reference substances and reference materials

Reference substances were either purchased from approved vendors or supplied by customers, initially tested, released, and stored in the required condition either in a desiccator or a refrigerator, and periodically monitored according to the following provisions:

- Instructed by manufacturer
- Verification of USP Reference standards retest date on the USP website, or other relevant websites, before each use.

Official pharmacopoeial standards were mostly used for the purposes described in the corresponding monographs. Adequate information was kept on the labels of reference substances. CoAs of Reference standards were available. An identification number was assigned to all reference standards and a person was nominated to be responsible for RS. An issue log was kept in which the required information was recorded.

The deficiencies identified on the reference materials were adequately addressed.

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 and the date when recalibration was due. Equipment were required to undergo DQ, IQ, OQ and PQ.

The balances were checked daily using internal calibration and regularly, using suitable test weights. Calibration was performed annually by a suitable service provider.

Records/logbooks were kept for the items of equipment with information to identify the device, current location, maintenance carried out, history of damage, malfunction, modification or repair. Use of the instrument was generally recorded. Calibration certificates were generally accepted by the laboratory.

Calibration certificates and qualification documentation of randomly selected equipment were reviewed and verified.

The deficiencies related to this section were adequately addressed.

13. Traceability

All calibrations or qualification of instruments were generally traceable to certified reference materials.

The traceability of samples from receipt, throughout the stages of testing, to the completion of the analytical test report was ensured.

The deficiencies on the traceability were adequately addressed.

14. Incoming samples

The laboratory was not involved in physical sampling. Samples were received from clients/markets, authorities, different hospitals in a "Receiving room" located in the laboratory facility before being transferred and stored in the sample storage room.

A test request accompanied each sample submitted to the laboratory to be agreed with the external customer. The test request contained the required information.

The test requests were reviewed by the laboratory manager to ensure that the laboratory had the resources to meet required specifications and that the selected tests/methods were capable to meet the customers' requirements.

All delivered samples and accompanying documents were assigned a lab code which was specific for the type of client (MEDS, internal or external clients). A register (excel spreadsheet) was maintained in which the following information was chronologically recorded:

- registration number of the sample,
- date of receipts,
- Tests to be performed.

Samples were stored in a storage room with restricted access and controlled temperature and relative humidity. Both maximum and minimum temperature were recorded daily. Visual inspection of samples was carried out by the sample custodian to ensure that labelling conformed with the information contained in the test request.

The record for sample with Amoxicillin and Clavulanate Potassium for Oral Suspension, was reviewed.

Samples were distributed to the analyst only in a quantity necessary for analytical run. If additional amount of sample was needed, a request would be sent to the sample custodian. The records were documented in the Sample issuance register. Samples were tested on a First in – First out order, unless an urgent test request was received. The deadline for test performance, from the day of receipt of sample to the date of dispatch of the report was 25 working- days which was monitored by the generation of a report to identify the deviations. A presentation of the last report was provided.

The deficiencies on the incoming samples were adequately addressed.

15. Analytical worksheet

The analysts recorded information about samples, test procedures, calculations and results in analytical worksheets, which were completed by raw data.

The worksheets contained the following information:

- the date on which the analysis was started and completed;
- reference to specifications and, in general, full description of the test methods, by which the sample were tested, including the limits; identification of test equipment used; reference substances, reagents and solvents employed;
- interpretation of the results and
- the conclusion whether the sample was found to comply with the specifications;

Values obtained from each test, including blank results, were required to be immediately entered on the analytical worksheet and all graphical data, whether obtained from recording instruments or plotted by hand, were attached or were traceable to the electronic record file or document where the data was available in accordance with the applicable procedure.

The completed analytical worksheets were signed by the responsible analyst and verified, approved and signed by the supervisor. For corrections, the old information was deleted by putting a single line through it. Alterations were signed by the person making the corrections and the date for the changes was inserted. The reason for the change should also be given.

The analytical worksheet and records of sample with Mebendazol Benzoate Suspension for Identification (FTIR), Deliverable Volume, pH, Assay of metronidazole benzoate (HPLC) and Limit test for Metronidazole (HPLC) were reviewed.

The deficiencies on the analytical worksheet were adequately addressed.

16. Validation of analytical procedures

SOP for Validation of Analytical Methods was reviewed. The laboratory implemented pharmacopoeial and manufacturer methods in chemical and microbiological analysis of medicines. These methods were used within the limits prescribed by the respective monographs, followed by method verification. Revalidation of analytical procedures was undertaken in the event of major changes in an analytical procedure.

Appropriate system suitability tests were employed prior to the analytical tests for verification of pharmacopoeial methods and/or validated analytical procedures.

The deficiencies on the validation of analytical procedures were adequately addressed.

17. Testing

Test procedures were described in detail and allowed analysts to perform the analysis in a reliable manner. Deviations from the test procedures were approved and documented.

Specific SOPs for sample analysis were reviewed.

Randomly selected sample testing documentation was reviewed:

The deficiencies identified on the testing were adequately addressed.

18. Evaluation of test results and OOS investigation

Results were reviewed by the Laboratory manager for approval prior to the inclusion of results on the Certificate of Analysis produced by the laboratory. The results and compliance with the internal QMS requirements were checked and verified. Certificates of analysis were issued by the laboratory based on information recorded in analytical worksheets.

A Work Instruction was in place describing the procedure to conduct investigations of OOS test results. A deadline corresponding 30 days was given to the investigator to close the investigation. OOS trending was performed quarterly to be presented for the management review. OOS investigation form was also reviewed.

Randomly selected analytical test report and OOS investigations were reviewed.

The test reports also included the following information:

- the background and the purpose of the testing;
- reference to the specifications and methods used;
- the results of all tests performed (or numerical result with the SD of all tests performed);
- the statement whether the sample complies with the requirements.

The deficiencies identified on the investigation of OOS were adequately addressed.

19. Certificate of analysis

A certificate of analysis was prepared for each sample/batch of a substance or product and contained series of information, among others:

- the results of the tests performed with the prescribed limits and
- a conclusion as to whether the sample was found to be within the limits of the specification.
- the date on which the tests were completed

The release of analytical reports and certificates of analysis was described in working instruction Certificates of Analysis.

The deficiencies identified on the Certificate of Analysis were adequately addressed.

20. Retained samples

Samples were submitted to the laboratory in a quantity required by the test request. Unused samples, including returned samples were retained in their final pack and in a separate room to be used in case of dispute. Samples were stored until one year after their expiry date.

21. Safety

Staff was wearing laboratory coats and goggles. Safety showers were installed. Safety data sheets were available before testing was carried out. The safety measures appeared to be properly implemented.

Handling of waste materials was addressed as per work instruction for Waste Disposal.

The deficiencies identified on the safety were adequately addressed.

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, ***Mission for Essential Drugs and Supplies (MEDS) – Quality Control Laboratory***, located at ***Mombasa Road, opposite Nation Printing Press; Viwandani, Nairobi, KENYA*** was considered to be operating at an acceptable level of compliance with WHO GPPQCL Guidelines.

All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the WHOPIR, were addressed by the manufacturer, to a satisfactory level, prior to the publication of the WHOPIR.

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

Part 4	List of WHO Guidelines referenced in the inspection report

1. WHO Good 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***
   http://www.who.int/medicines/publications/44threport/en/

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. Fourth-Sixth Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2.
   Short name: WHO TRS No. 970, Annex 2
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/
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. Guidance on good data and record management practices. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5.
   Short name: WHO GDRMP guidance or ***WHO TRS No. 996, Annex 5***
   http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf

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***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/
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://www.who.int/medicines/publications/44threport/en/

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

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** http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_1010/en/

14. 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/

15. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013 (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/

16. WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (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

17. 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

18. 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***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

19. 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***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

21. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4. ***Short name: WHO TRS No. 937, Annex 4***
http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf?ua=1

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