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

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<tr><td>Introduction</td><td></td></tr>
<tr><td>General information</td><td>The Public Health Laboratory Dr. Giovanni Cysneiros (LACEN-GO) has been in operation since 1947. It had two areas of activity, the Medical Biology Coordination section with the function of contributing to the prevention, control and monitoring of diseases, in attention to the actions of epidemiological surveillance and medical assistance, and the Products and Environment Coordination section that monitors the quality of food, water, medicines,</td></tr>
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	cosmetics, sanitizers and other products subjected to sanitary and environmental surveillance. The Drug Service, a subsection of the Products and Environment Coordination section, was established in 1999 and has been executing quality control of pharmaceutical products, performing physical-chemical assays (identification, content, dissolution) and microbiological tests.
History	This was first WHO inspection. In addition the Laboratory was inspected by: • National Health Surveillance Agency (ANVISA) • Municipal Health Surveillance System
Scope and limitations	
Areas inspected	See Part 2 below
Restrictions	N/A
Out of scope	N/A

Abbreviations

AHU	air handling unit
ALCOA	attributable, legible, contemporaneous, original and accurate
API	active pharmaceutical ingredient
BDL	below detection limit
CAPA	corrective actions and preventive actions
CC	change control
CFU	colony-forming unit
CoA	certificate of analysis
DQ	design qualification
EM	environmental monitoring
FAT	factory acceptance test
FMEA	failure modes and effects analysis
FPP	finished pharmaceutical product
FTA	fault tree analysis
FTIR	Fourier transform infrared spectrometer
GC	gas chromatograph
GMP	good manufacturing practice
HACCP	hazard analysis and critical control points
HPLC	high-performance liquid chromatograph
HVAC	heating, ventilation and air conditioning
IR	infrared spectrophotometer
IQ	installation qualification
KF	Karl Fisher
LAF	laminar air flow
LIMS	laboratory information management system
LoD	limit of detection
LOD	loss on drying
MB	Microbiology

MBL	microbiology laboratory	
MR	management review	
NMR	nuclear magnetic resonance spectroscopy	
NRA	national regulatory agency	
OQ	operational qualification	
PHA	process hazard analysis	
PM	preventive maintenance	
PQ	performance qualification	
QA	quality assurance	
QC	quality control	
QCL	quality control laboratory	
QRM	quality risk management	
RA	risk assessment	
RCA	root cause analysis	
SOP	standard operating procedure	
TAMC	total aerobic microbial count	
TFC	total fungi count	
TLC	thin layer chromatography	
URS	user requirements specifications	
UV	ultraviolet-visible spectrophotometer	

Part 2	**Brief summary of the findings and recommendations (where applicable)**

Brief summary of the findings and comments

1. Organization and management

The laboratory was legally authorized with managerial and technical personnel to oversee the quality management system and oversee the procedures for performing tests and/or calibrations, validation and verification, and to initiate corrective actions when required. Management and personnel were civil servants and had to comply with Goiás State Civil Servant law No 10.460.

Roles and responsibilities were specified in signed job descriptions.

The SOP "Data and information confidentiality" was briefly discussed. Confidentiality agreements were signed when employees joined the laboratory.

The laboratory maintained a registry for receiving, distributing and supervising the consignment of the samples to the specific testing units; and keeping records on all incoming samples, analytical worksheets, certificates of analysis and accompanying documents.

2. Quality management system

Generally, the Quality Management System covered aspects according to good practices for pharmaceutical quality control laboratories. The contents included e.g. contracts, purchasing services, non-conforming testing, corrective actions, complaints, personnel, protection of confidential information.

The Quality Management System (QMS) covered all activities of the laboratory. It was based on ABNT NBR ISO/IEC 17025: 2005 with reference to WHO guidelines on good practice for pharmaceutical quality control laboratories and good practice for pharmaceutical microbiology laboratories.

The quality management system was supervised by the Director General (DG) and all SOP of the Quality Management System was approved by the DG.

The QMS documentation included Quality Manual, Biosafety Manual, Standard Operating Procedures, Technical Reports, Form of Records, Certificate of Calibration, analytical reports and external documents, such as: legislation, technical standards, and official methods.

The Quality Manual was approved and signed by the Director General and contained a commitment to establish, implement and maintain an effective quality management system and compliance with standards of good practice.

Quality Manuals and Quality Policy were briefly discussed. The QMS was developed during the last four years. Several SOPs were recent and some records sheets were enforced early 2018.

The quality management system SOPs listed below were briefly discussed:

- The SOP "Publication of standard operating procedures". The list of SOPs was presented to the inspectors
- The SOP "Elaboration of Manual and Operational Standardized Procedures"
- The SOP "Control of Nonconforming Products and Services, corrective action and preventive action"
- The SOP "Control of laboratory and administrative technical records"
- The SOP "Guidelines for Validation of Analytical Methods"
- The SOP "Contracting and monitoring of suppliers". This SOP was applicable for evaluation of external suppliers of materials and services what could affect quality of tests. Forms XX were used for suppliers monitoring.
- The "Internal and external customer's complaints". Complaints could be received by any employee, registered in the form XX and forwarded to the Quality Management. There were no complaints received addressing Drug Service.
- The SOP "Internal audits". According to the SOP internal audits should be performed annually. Annual internal audit program for 2017 was presented to the inspectors. Audits were performed by qualified internal auditors. List of internal auditors was presented to the inspectors. Conflict of interest was avoided; auditors were not allowed to audit their own departments. Last internal audit of Drug Service was carried out XX. Audit report was discussed, it listed non-conformities. CAPAs were proposed by Quality and Section Coordinators. Implementation of CAPAs was checked by representative of Quality Department.
- The SOP "Control of CAPAs and non-conformities" and form XX "Non conformity record". SOP also explained dealing with CAPAs and improvements. The SOP was applicable, but not limited to:
    - Samples
    - Processes
    - Equipment
    - Facilities
    - Internal audits

The Form XX was used to record:
- Complaints
- Non-compliant products
- Non-compliant service
- Preventive actions
- Non-compliance to guidelines or procedures
- Internal audits

Root cause analysis related to the non-conformities was carried out by Quality Coordinator and Coordination of the department. It was explained that tool similar to the 5 Whys was used for RCA, but this was not specified in the SOP

- The SOP "Change control" and form XX "Control of changes". SOP and was applicable, but not limited to the following, changes:
  - Process
  - Infrastructure
  - Systems/Utilities
  - Equipment/instruments
  - Analytical methods
- The SOP "Critical analysis". Critical analysis was defined as a formal review of key performance indicators of QMS carried out by high management. Critical analysis review meeting should be carried out annually but not exceeding 15 months. Last critical analysis review was carried XX. List of participants and meeting agenda was presented to the inspectors. SOP contained section on standard meeting agenda. Agenda covered the following items:
  - Suitability of policies and procedures
  - Personnel management
  - Internal audit outcome
  - CAPAs
  - External organisations audits
  - Outcome of proficiency testing
  - Implementation of new methodologies
  - Customer feedback
  - Complaints
  - Recommendations for improvement
  - Other relevant factors. For example activities of QC, resources and training

3. Control of documentation

Documented procedures were in place. Authorized SOPs Master List identifying current version, status and distribution of documents was available and presented to the inspectors. It was identified that the document presented was not a controlled document and not identified as uncontrolled. Documents were available in LACEN-GO's network as PDF files which couldn't be altered. A system of document control was in place to withdraw obsolete documents and to inform staff of new and revised procedures.

Documents had a unique identification number, version number and date of implementation but no revision date.

One paper controlled copy, stamped, dated and signed was available at the Quality Department for QMS procedures. For other procedures, used in the department daily work, one controlled copy was also available in the department at the place of use.

The SOP 63.1040-19 "Control of procedures and documents of the management system of the Quality Review" were briefly discussed. The Quality documents were controlled in order to preserve the physical integrity, availability of contents and traceability.

4. Records

Original observations, calculations and derived data, calibration, validation and verification records and final results, were retained. The records included the data recorded in analytical worksheets. The records included the identity of the personnel involved in the sampling, preparation and testing of the samples.

Change control was not applied to the modification of documents and records. When a revision of a document was deemed necessary, the request was done by e-mail by the respective department to the QMS requesting the document to be made available, by the coordinator of the QMS, in a shared electronic folder. The QMS manager made the master document available in the specific folder. After the change was incorporated by the department, it was forwarded to the QMS coordinator who uploaded the new revised document in the system.

Dossiers containing information starting from sample receipt and analytical raw data were stored in laboratory for 15 years; 5 years in Drug Service laboratory and 10 years in Institute archive. Documents were stored in laboratory office drawers in good order.

5. Data processing equipment

HPLCs, UV and IR instruments were linked to computers operated by their respective software. All raw data generated by these instruments were stored as hard copies and electronically on a server. Hard copies of raw data were kept; the system was in place to back-up the raw data from the server.

The SOP "Information Security Procedure of medicines, cosmetics, sanitizers and health products " requested all relevant electronic data to be backed up at two different location every Sunday. One data back-up was kept in the department where the laboratory was located and another back-up was saved in a different folder at the IT building. All backups were done automatically by the software Iperius Backup® which was a commercial backup system validated by the supplier and installed recently replacing an obsolete system. Every Monday the actual back-ups were verified by an analyst and registered in the record form XX as detailed in the procedure.

6. Personnel

Generally the laboratory had sufficient personnel with the necessary education, training, technical knowledge and experience for their assigned functions. Staff members undergoing training were supervised and were assessed on completion of the training. Personnel performing specific tasks were appropriately qualified in terms of their education, training and experience, as required. Current and detailed job descriptions were maintained.

Personnel were identified to perform critical activities such as sample processing, reagent preparation, qualification, verification and maintenance of instruments.

When internal training was given as initial training or for new activities or new equipment, a recent procedure SOP "Internal Training" implemented in October 2017 required daily assessment. The training and the daily evaluation result were recorded on Form XX.

The SOP "Human Resources Activities" was briefly discussed.

The SOP "Capacity Building and Resource Development Program Human Resources of LACEN-GO" made provision for the identification of training needs.

A number of personnel files including job descriptions were briefly discussed.

The list of training needs identified for 2017 and subsequent training plan for 2017 was presented to the inspectors as well as the summary of trainings actually performed in 2017 or those postponed to 2018.

The laboratory site employed 12 persons.

7. Premises

Generally Drug Service laboratory facilities were of a suitable size, construction and location, with the exception of the Drug microbiology laboratory. Rest and refreshment rooms were separate from laboratory areas. Laboratory had storage facilities for storage of samples, reagents and glassware. Temperature and relative humidity in sample storage was checked twice per day.

Microbiological testing was performed in a separate laboratory which consisted of two rooms – general room for documentation and incubation and one room where the biosafety cabinet was located. It was explained to inspectors that work with master stains and products were done in different days to avoid contamination and cross-contamination. Environmental monitoring of biological Safety Cabinet was carried during the tests.

8. Equipment, instrument and other devices

Generally the laboratory had test equipment, instruments and other devices for the performance of the tests and/or calibrations, validations and verifications. Calibration status labels were attached to instruments. All laboratory instruments had "instrument log books".

Laboratory used class "A" glassware, which was verified every two and a half years in-house and calibrated every 5 years by external agency.

Temperature in the Microbiology Laboratory the incubators and refrigerators were monitored daily and was controlled twice per day.

The last performance qualification record of the dissolution test equipment was briefly discussed. The cleaning of the dissolution equipment was described in the SOP "Operation of the dissolution equipment SR8 plus".

The SOP "Cleaning of the equipment and glassware" was briefly discussed. The procedure proposed to use two types of detergents, one domestic and one specific to laboratories but didn't give additional useful information with specific cleaning instructions given in the equipment usage SOPs.

9. Contracts

Contracts with service providers were available. The contract with the service provider "XX" (calibration / verification / preventive maintenance) was briefly discussed. This contractor provided service for simple instruments, like agitators, balances, pipettes with calibration and maintenance of more sophisticated laboratory instrument such as HPLC, FT IR and UV VIS spectrometer outsourced to a third party as was the case for HPLC calibration and maintenance contracted to Agilent.

Laboratory tests were not outsourced to another laboratory.

10. Reagents

Laboratory reagents were purchased centrally via tenders. Reagents had specific identification codes and specifications listed in the state program COMPRAS NET. This program was used for purchase of reagents.

The SOP "Materials receiving and distribution" was briefly discussed. Reagents were delivered together with invoices, certificates of analysis and MSDS (hard copies and electronic copies). Upon receipt technician from warehouse and Drug Service compared order and received reagents. Check list was used for reagents receipt. All reagent containers were visually inspected. Reagents were received at the central store and distributed to the laboratories. All reagents had expiry dates. The state electronic program SIGMATE was used to maintained reagents inventory, with stocks regularly monitored.

Solutions prepared by the laboratory were labeled and stored appropriately with preparation records available and traceable to the reagent batch/lot numbers and expiry dates.

The SOP "Preparation and standardization of laboratory solutions" was briefly discussed. Preparation of reagent solutions was recorded in the Form XX. Preparation and standardization of titrimetric solutions was recorded in the Form YY.

Water supplied by a Purelab Ultra system was used to prepare HPLC buffer solutions. Conductivity and TOC were monitored on-line. Microbial tests on water was carried out once per month. Purified water was used for solution preparations.

Media used in the Microbiology Laboratory was prepared within the LACEN GO by the Media culture preparation department. Growth promotion (GP) test was performed on every batch and on every shipment of dry Media. GP tests were not performed in the Media culture preparation department. GP test for dry Media and liquid media used in microbiological section of Drug Service was performed in the Microbiological laboratory.

Media was sterilized according to the manufacturer's specifications e.g. 121°C for 15 minutes. Autoclave qualification was carried out annually by an external service provider.

Dry Media were visually checked upon receipt followed by additional checks using a check list. Media was received with the manufacturers CoA.

11. Reference substances and reference materials

A reference substances register and usage log books were available and traceable to the analysis used for. The Laboratory used only Pharmacopoeia reference substances mainly from the Brazilian Pharmacopeia. The SOP “Control of reference materials” was briefly discussed. SOP was applicable to reference substances, standard weights and buffer solutions. The Brazilian Pharmacopeia reference substances web page was checked every two months and before usage of the standard.

The SOP "Control of Reference Material” and related personnel training records were briefly discussed. Reference standards and substances were purchased by the technical directorate.

Reference standards were stored in the chemical laboratory in a lockable cabinet (room T) or lockable fridge. Temperature was controlled twice per day. Temperature mapping of the fridge was done annually.

Reagents and solvents, acids and bases were stored in the reagent storage room. Only limited quantities of these materials were kept in the laboratory.

In the Microbiology Laboratory reference cultures were obtained from the National Institute of Health Quality Control (INCQS). The strains were originally derived from ATCC strains. No more than 5 subcultures were used from the original source strain.

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

Generally the laboratory had test equipment, instruments and other devices for the performance of the tests and/or calibrations, validations and verifications. Calibration status labels were attached to instruments. All laboratory instruments inspected had “instrument log books”.

The SOP “Management of laboratory instruments and equipment in Drug Service” was briefly discussed. SOP specified laboratory calibration and verification frequency. Analytical balances were verified daily or before use, monthly and every six months. HPLCs, dissolution instrument UV/VIS spectrophotometer, FTIR and automatic pipettes were verified every three months.

The SOP “Equipment Control and the SOP “Calibration Plan” were briefly discussed.

The SOPs “Procedure for preparing, validating and using spreadsheet of electronic calculation” and SOP “Mean weight determination and Calculation of measurement uncertainty” were briefly discussed. Validated excel sheets were used for calculation of analytical results. Verification of excel sheets was performed annually.

13. Traceability

Test results were traceable to analyst, analytical instruments, equipment, reagents, reference substances and test procedures.

14. Incoming samples

The SOP "Sample flow up to certificate of analysis issuance" was briefly discussed. Samples were received by responsible persons at sample reception. Check list "Receiving and checking the samples" was used. It contained the following sections:

- Place of collection
- Product identification
- Sample collection form
- Sample evaluation

The laboratory had a central registry dealing with registration and distribution of samples. The SOP "Sample acceptance and rejection" was discussed. Samples were received form:

- Department of Health
- Regional Health Units
- Health surveillance Units
- Public prosecutor office

Samples were received in sealed bags. Three sets of samples were collected by supervisory bodies. One set of samples was stored at the place of collection and two sets were received by the laboratory. One set was sent for analysis and one was kept as a retention sample.

Records of incoming samples were properly kept for all incoming samples according to the SOP by logging it in an electronic register using HARPYA software provided by the INCQS (national institute of quality control in health). Individual samples were labelled by the laboratory.

Each individual sample had attached a label indicating the HARPYA number. Labelling of samples was done by the laboratory.

The SOP "Sample flow of samples until the analytical report is issued" and SOP "Quality Assurance of Results" were briefly discussed. Incoming samples were analysed in accordance to the "Test Request Form". Samples received from the Federal State Municipal surveillance program had no "Test Request Form" as the program required specified tests to be done.

Sample identification numbers were recorded on all documents; forms, test reports, CoA, etc.

15. Analytical worksheet

Analysts recorded tests performed, raw data, calculations and results in analytical work sheets. Calculations were checked by a second analyst. Sufficient details were recorded in analytical work sheets to establish traceability. This was confirmed by verifying the Bromoprida 4 mg/ml oral solution sample and documents file.Verification of dossier including analysis of raw date was performed by the Coordinator Drug Service.

16. Validation of analytical procedures

Microbial enumeration tests were verified for each product to be analyzed. The SOP "Verification of microbiological enumeration test method" was briefly discussed. Bromoprida solution method verification was inspected. All microorganisms as per the pharmacopoeia requirements were used.

The SOP "Guidelines for Validation of Analytical Methods" and SOP "Verification of pharmacopoeia methods" were briefly discussed.

17. Testing

The samples were tested in accordance with the state surveillance program. Test results were recorded in the analysts' analytical work sheets. Tests were performed following either the pharmacopeia methods or manufacturer's methods.

Proficiency testing scheme

The SOP "Quality assurance of the results from Drug service, cosmetics, sanitizers and health products" explained participation in proficiency testing schemes.

The Laboratory participated in the National Institute of health Quality Control – INCQS proficiency testing scheme as well as in the control lab proficiency scheme.

18. Evaluation of test results

Test results were discussed and evaluated after completion of all the tests. The evaluation took into consideration the results of all tests. When doubtful (atypical results obtained) they were investigated.

The SOP "Quality assurance of the results from Drug service, cosmetics, sanitizers and health products" was briefly discussed. Objective of this SOP was: identify, define and evaluate the procedures used to ensure the quality of analysis. Analytical test results were verified by another experienced analyst using the check list. Section XX of the SOP explained evaluation of OOS results. OOS were evaluated by the Coordination Drug Service using a check list for either chemical analysis or microbiological analysis.

19. Certificate of analysis

The SOP "Issuance, forwarding and filing of certificate of analysis" was briefly discussed. Analytical results were transferred by analysts to the HARPYA system to create draft CoA. Afterwards Drug Service coordinator verified draft CoA and signed the draft. Draft was also signed by analyst. Final CoA was printed and approved/signed by Product Decision coordinator and Technical Director.

20. Retained samples

The SOP "Storage, distribution and discharge of samples" was briefly discussed. Retain samples were stored in sample storage room in locked cabinets. If analysis was satisfactory, samples were discharged within 90 days. In case sample test results were not satisfactory, retained samples were kept till the expiry date.

21. Safety

Safety data sheets were available to staff before testing was carried out; smoking, eating and drinking in the laboratory was prohibited. Staff wore laboratory coats and used eye protection. Safety showers were installed.

PART 4 CONCLUSION

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, as well as the corrective actions taken **Secretary of Health – State of Goiás Public Health Laboratory Dr. Giovanni Cysneiros Drug Service, located at Av. Contorno, 3556 – Jardim Bela Vista – Goiania Goias CEP:74853-120 Brazil**,was considered to be operating at an acceptable level of compliance with WHO Good Practices for Pharmaceutical Quality Control Laboratories for the following expertise:

Type of Analysis	Finished Products
Physical / Chemical analysis	pH, water content, loss on drying, density, dissolution, friability, uniformity of dosage units (mass content)
Identification	FTIR, TLC, HPLC (UV-VIS, Dad, fluorescence detection), UV-vis spectrophotometry, basic tests
Assay, impurities and related substances	HPLC (UV-VIS, Dad, fluorescence detection), TLC, UV-vis Spectrophotometry, FTIR, volumetric titrations, potentiometry, determination of related substances / impurities, degradation products
Microbiological tests	Microbial limit test

PART 4

List of GMP guidelines referenced in the inspection

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 TRS No. 961, 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 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 TRS No. 986, Annex 2
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

4. 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/

5. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (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

6. WHO guidelines on good manufacturing practices for heating, ventilation and air-conditioning systems for non-sterile pharmaceutical dosage forms. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 5
Short name: WHO TRS No. 961, Annex 5
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

7. 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

8. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert 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/

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. 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/

14. 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

15. 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 TRS No. 996, Annex 5
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf