World Health Organization

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

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

Part 1	**General information**
Laboratory Details	
Name of the laboratory	The Testing Laboratory of Territorial Branch of the Republic State Enterprise Founded on the Right of Economic Management «National Center for Expertise of Medicines and Medical Devices» of the Committee for Quality Control and Safety of Goods and Services of the Ministry of Health of the Republic of Kazakhstan in the City of Karaganda – (Karaganda)
Address of inspected laboratory	9A Bukhar Zhyrau Prospect Karaganda City Karaganda Region Republic of Kazakhstan Tel: + 8 (7212) 41-31-68 Fax: + 8 (7212) 41-31-68 E-mail: karaganda@dari.kz Website: www.ndda.kz
GPS Coordinates	Latitude: 49.8160 Longitude: 73.0779
Inspection details	
Dates of inspection	17-19 June 2019
Type of inspection	Initial
Introduction	
Brief description of testing activities	See table below

Type of analysis	*Finished products*	*Active pharmaceutical ingredients*
Physical/ Chemical analysis	✓ pH ✓ Loss on Drying ✓ Water Content (Karl Fisher) ✓ Dissolution ✓ Uniformity ✓ of dosage (mass or content) ✓ Volume	✓ pH ✓ Loss on Drying ✓ Water Content (Karl Fisher), ✓ Sulphated ash ✓ Acid ✓ insoluble ash ✓ Residual solvents.

		✓ Uniformity of dosage units (mass, content), ✓ Disintegration ✓ Hardness	
	Identification	✓ HPLC (high performance liquid chromatography) ✓ GC (gas chromatography) ✓ Spectrophotometry (UV-Vis) ✓ Basic tests	✓ HPLC ✓ GC ✓ Spectrophotometry (UV-Vis) ✓ Basic tests
	Assay, impurities and related substances	✓ HPLC ✓ GC ✓ Spectrophotometry (UV-Vis) ✓ Titrations	✓ HPLC ✓ GC ✓ Spectrophotometry (UV-Vis) ✓ Titrations
General information	The accredited testing laboratory is a national quality control laboratory which provides analytical services for the quality and safety of medicines and medical devices in the Republic of Kazakhstan. The accredited testing laboratory is a structural subdivision of the territorial branch of the Republic State Enterprise founded on the Right of Economic Management «National Center for Expertise of Medicines and Medical Devices» of the Committee for Quality Control and Safety of Goods and Services of the Ministry of Health of the Republic of Kazakhstan in the City of Karaganda. The accredited testing laboratory aims to provide quality testing services for medicines and medical devices to private manufacturers and suppliers. The testing services provided by the testing laboratory are required to comply with the guidelines of World Health Organization (WHO) Good Practices for Pharmaceutical Quality Control Laboratories (GPQCL) [WHO Technical Report Series, No. 957, 2010], relevant part of WHO Good Manufacturing Practices (GMP) and international standard ISO/IEC 17025-2017, General Requirements for the Competence of Testing and Calibration Laboratories.		
History	The laboratory was accredited by National Certification Center LLP in accordance with the requirements of GOST ISO/IEC 17025-2009, with accreditation certificate No. KZ.И.10.0233 dated 11 February 2014. The laboratory was reaccredited on 12 June 2019, with accreditation certificate No. KZ.T.10.0233.		

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	- Organization and management - Quality Management System - Data processing - Premises: Physico-Chemical laboratory - Evaluation of test results, including investigation of OOS - Personnel, including training and safety - Documentation and Records - Equipment – Calibration / Qualification – Performance check - Validation and verification of the methods - Traceability and records - Sample and material management, including water qualification - Suppliers and contractors
Restrictions	None
Out of Scope	Microbiological laboratory
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
TL	Testing Laboratory
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 country was presented by five territorial Quality Control Laboratories with the Head office (Laboratory Test Centre) in Nur-Sultan and three representative offices.

The laboratory in Karaganda had defined the organization and management structure of the laboratory; i.e. responsibility, authority and interrelationship of the personnel, in their organogram. The total number of staff accounted to 26 at the time of inspection. The laboratory was headed by Dr. Zeinelov Timur Sansyzbaevich. The relationship between the positions and activities were illustrated on the organizational chart. The Quality Manager was reporting to the Director of Territorial Branch.

The laboratory comprised of the following sections:
- Management
- Department of safety and quality assessment of drugs and Medical Device
- Physical and Chemical Department of the Testing Laboratory
- Bacteriological Department of the Testing Laboratory
- Toxicological Department of the Testing Laboratory

The laboratory had arrangements to ensure that its management and personnel were not subjected to commercial, political, financial and other pressures or conflicts of interest that may adversely affect the quality of their work. The laboratory had a policy in place to ensure the confidentiality of information contained in marketing authorizations and test reports.

The deficiencies identified on the organization and management were adequately addressed.

2. Quality management system

A quality manual defining the quality management system was available. The quality manual defined the policy, goals and objectives related to the quality. The quality policy statement was an integral part of this manual. The quality manual described the hierarchy of the documented procedures, work instructions, standard operating procedures, and test methods.

The system of the TL (Testing Laboratory) documentation consisted of four levels:

Level 1 Quality Manual (included the quality policy and objectives, mission);
Level 2 Documented procedures (administrative and technical)
Level 3 Working instructions, standard operating procedures (hereinafter the SOPs), test methods, job descriptions;
Level 4 Records and forms (administrative and technical: accounting records, reports, log-books, etc.).

The TL took part in the collaborative trials organized by the Testing Center (chief laboratory) of the RSTF on the REC.

Management Review:
The most recent Management Review meeting took place on 12 Feb 2019 in accordance with the applicable SOP, containing all the required topics. The results of the entire year 2018 was presented for the Management. Recommendations from the Management Review were managed by the Quality Person.

Internal audits:
The activities of the laboratory were systematically and periodically audited internally. Management reviews were performed annually, covering audit reports, complaints and proficiency testing.

The testing laboratory had established a system of planned and documented internal audits to verify the laboratory's quality system and technical operations in accordance with SOP titled "Internal Audits". Internal audits were conducted by trained internal auditors based on a schedule established by the Quality Manager. The annual internal audit schedule contained all the elements of the QMS, including testing and calibration activities.

The TL's internal audit findings were compared to the internal policies and procedures, as well as ISO/IEC 17025 standard requirements. Any deviation from internal policies and procedures or the ISO standard were identified and addressed accordingly. The implemented Corrective Actions were reviewed and evaluated by the TL under supervision of the Quality Manager as per the applicable SOP. The audit plan for 2019 and the latest audit report were reviewed. Since no observation was made, a CAPA plan was not applicable.

Change control
Change control SOP with respective template was implemented on 18 Mar 2019. Change control procedure applied to any changes within the laboratory activities.

The deficiencies identified on the QMS were adequately addressed.

3. Control of documentation

The laboratory had established and maintained a system of procedures that allowed review and control of all procedures (preparation, revision, distribution, return, archiving) as per the requirements.

SOP titled "Document Management" applied to the process of managing internal and external documentation. In accordance with this procedure, management of all documents of the management system, either developed in the TL or received from outside; i.e. regulations, standards, regulatory documents, test methods, software, specifications, instructions and user guides, was assured.

A master list identifying the current revision status and distribution of documents in the QMS was provided. The master list was annexed to the LIF.

Responsibility for maintenance of documentation in force in TL and timeliness of withdrawal from outdated documents was borne by a quality specialist.

The logbooks were compiled as per the forms specified in the QMS documents. The quality specialists prepared the logbooks for work, i.e. tying, numbering, and approval by the responsible person. When providing a logbook to a specialist, the designated person recorded the data in the Logbook for Logbook Registration.

The deficiencies identified on the control of documentation were adequately addressed.

4. Records

A procedure was established for identification, collection, filing, indexing, access, storage, maintenance, withdrawal, and disposal of the records concerning the management system and technical activities of the Testing Laboratory, i.e. SOP for “Control of records”.

The records were completed and signed, alterations were commented, and references were made to appendices containing the relevant recordings, e.g. chromatograms and spectra. Records were kept in an archive for a period of shelf-life, in an orderly manner. Access to the archive was restricted to authorized personnel, only. The preventive measures to avoid early destruction of records and documentation were implemented.

5. Data processing equipment

An inventory of all computerized systems was requested. Master plan for validation of computerized system was available in accordance with a working guideline; dated 18 Mar 2019. However, the required information was not sufficiently captured on the plan. The risk assessment of the software systems used for HPLC activities was described in the SOP titled as "Analysis of Risk function of the computerized system of HPLC". The SOP for risk assessment was also presented.

Electronic data was backed up at appropriate regular intervals according to SOP titled as "Integrity of data – Backup". Generated data on the chromatography software system were automatically stored on a server using Exiland backup Free 4.4 program. The program was installed on each computer and the activity was verified daily. The USB portals at the workstations were deactivated. The workstations were not connected to the internet.

Concerning spreadsheets, all cells including calculations were locked so that formulas could not accidentally be overwritten. Free access was only given to cells to be filled in, with data. Calculation algorithms were tested with another validated software or by a pocket calculator. The sheets were made available in a secured directory.

The laboratory used an electronic information management system "Safety Assessment and Quality of Medicinal Products, Medical Devices (SQAD)", which had passed the test at NCEMMD and was protected through a dedicated VPN channel. Entry into the information system "Safety and quality assessment of drugs, medical devices" was provided by individual logins and passwords to authorized personnel only. SQAD was used to register the sample testing applications, regulatory documentation (i.e. specifications and test methods), and CoAs after completing of testing.

Other database systems were also used in the laboratory:

- For the management of the reagents' use
- For designation of analyst to the respective sample test request, supervision of sample testing deadlines and registration of CoAs.

The management of computer hardware and software, including the integrity, confidentiality of input, collection, storage, transmission and processing of data, was described in SOP titled as "Data integrity for the integrity and protection of laboratory testing data".

Windows XP operated computerized systems were not supported by Microsoft Software any longer.

The deficiencies identified on the data processing equipment were adequately addressed.

6. Personnel

The laboratory had sufficient personnel with the necessary education, training, technical knowledge and experiences for their assigned functions. Training of staff and the respective assessment after completion of training were described in detail in the applicable SOP. A competency matrix consisting of four analysts was available and a reassessment was carried out annually. The laboratory maintained current job descriptions for all personnel involved in tests and/or calibrations, validations and verifications. The laboratory also maintained records of all technical personnel, describing their qualifications, training and experience. Staff SOP training was documented on a template, attached to the master copy of the respective SOP. All staff were on permanent contract and their working hours were from Monday through Friday from 9 am to 5:12 pm.

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. The physico-chemical was well-organized and well-maintained. 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) conditions. The environmental conditions of these rooms were monitored and controlled. Gases were stored in a dedicated store. The laboratory provided separate rooms for storing flammable substances, fuming and concentrated acids and bases.

Access to the laboratory facilities was restricted to designated personnel by individual key cards.

The deficiencies identified on the premises were adequately addressed.

8. Equipment, instrument and other devices

Randomly selected 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 were available.

The following equipment and/or related qualification documentation were reviewed to verify the adequacy of their calibration/validation certificates:

- Qualification records of exhaustive hoods (the supply system).
- The periodic performance verification of HPLC instrument, as well as the qualification documentation of the associated software system
- The periodic performance verification of disintegration instrument, as well as the logbook for usage and maintenance
- The periodic performance verification of pH-meter, together with the logbook for the daily check and pH buffer used for titration solution.
- The balance room and the balances; 2 analytical and 1 technical balance

- Temperature mapping of one of the refrigerators.
- The periodic performance verification of UV-Visible spectrophotometer (repeated every year)
- The periodic performance verification of Karl-Fischer.
- Last annual requalification of Infra-Red equipment installed on June 2008
- The logbook of dissolution test equipment (Erweka)
- Milli-Q water purification system

The deficiencies identified on premises, instrument and other devices were adequately addressed.

9. Contracts

The selection and purchasing of services and supplies were handled centrally by a dedicated department in the State Head Office.

Pest control contract / technical specifications with service provider and associated invoice dated 12 Jun 2019 were reviewed.

The deficiencies identified on the contracts were adequately addressed.

10. Reagents

The reagents used with in the laboratory were of appropriate quality and correctly labelled. Labels of reagent contained: content, manufacturer, date received and date of opening of the container, concentration, if applicable, storage conditions, expiry date and retest date, as justified. Reagent and volumetric solutions prepared in the laboratory were also properly labelled.

Two types of water qualification were produced to be used for the following activities:

- 1st system for production of purified water to be used for washing of glassware
- 2nd system (Milli-Q water purification system) for production of highly purified water to be used for HPLC and reagent solutions.

The quality of water was verified weekly to ensure that the qualification of the highly purified water met the appropriate specifications by testing parameters such as pH, dry residue, heavy metals and different salts in accordance with the applicable SOP. The records were properly documented in the respective logbook along with the acceptable range.

The usage and management of columns was carried out in accordance with WI titled as "Management of chromatography columns"; dated 18 Mar 2019. One analyst was designated to monitor the use and storage of columns. Each column had a respective template with a name and an individual specification number. The sample identification and return date were also recorded on the template.

11. Reference substances and reference materials

Reference substances were provided for single use only. The remaining quantity was returned to the lab-technician to be discarded and recorded. They were initially tested, released, stored and monitored according to the provisions documented in the applicable SOP. They were stored and used in a manner that did not adversely affect their quality. Official, pharmacopoeial standards were used for the purposes described in the corresponding monographs.

All required information was kept on the labels of reference substances. The receipt and usage of the RS were documented on an Excel spreadsheet stored on the desktop belonging to the lab-technician with restricted access. In case of absence, a replacement was appointed in advance to handle the RS. The identification number was quoted on the analytical worksheets whenever the reference substance was used.

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. Balances were checked daily using internal calibration procedure and suitable test weights. Requalification was performed annually using certified reference weights.

Use of the instrument was recorded in assigned logbooks.

For more details, refer to the section 8 of this report.

Traceability

Test results were traceable, and where appropriate, references to the primary reference substances was available.

13. Incoming samples

Samples were received through the Safety and Quality Assessment Group for Medicines and Medical Devises (SQAG) of MCEMMD Karaganda. They received samples, with a registration number, to be analysed for three different purposes:

- Dubious samples
- For Pre-registration purposes; from manufacturers through e-application system
- For Post-registration purposes; batch analysis; from distributors though e-application system

Samples were recorded in respective logbooks and a test request accompanied each sample submitted to the laboratory and contained the following information:

- description of the sample
- specification to be used for testing
- required storage conditions
- Stamped, dated and signed by designated officer

The test requests were reviewed by the laboratory to ensure that the laboratory had the resources to meet the required specifications. In case of absences of resources such as equipment, RS and/or reagents, the sample was sent to another laboratory in accordance with SOP titled as "The conclusion on subcontracting for test of samples"; effective 2 May 2019.

All delivered samples and accompanying documents were assigned a registration number. A register was kept in which the following information was recorded:

- registration number of the sample
- date of receipts
- unit to which the sample was forwarded

Prior to testing, the samples were stored safely, considering the storage conditions for the sample. The samples were sent for testing to the specific unit. Specifications were provided in the General Method Descriptions, centrally uploaded in the "Evaluation of Safety and Quality software system" for registered medicinal products. The system was password protected.

The samples were divided into two portions upon receipt, based on a quantity assessment:

- Immediate testing
- For retention in case of dispute

Visual inspection of samples was carried out by the designated person to ensure that labelling conformed with the information contained in the test request. Only one employee was responsible for sample storage which had made the activity vulnerable in the absence of the responsible person.

The deficiencies identified on the handling of samples were adequately addressed.

14. 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
- ID no of the letter and date
- Name of department
- Sample ID no and name of product, as well as manufacturer's name
- Type of testing and the related specifications
- Interpretation of the results
- The conclusion whether the sample was found to comply with the specifications
- Any deviation from the prescribed procedures

Randomly selected analytical worksheet and/or OOS investigations were reviewed.

All values obtained from each test, including blank results, were immediately entered on the analytical worksheet and all graphical data, whether obtained from recording instruments or plotted by hand, were attached and were traceable to the electronic record file or document where the data was available.

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 was also given.

15. Validation of analytical procedures

The procedures employed for testing were fit for the intended use, since only pharmacopoeial methods were used for all the samples (only registered products). The pharmacopoeial methods were not used for any other purposes than the one it was established for. However, SOP on "Validation and verification of methods" was available.

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

16. Testing

Test procedures were described in the test methods which were centrally uploaded in a respective software system and allowed analysts to perform the analysis in a reliable manner. Specific tests were carried out by another unit or by specialized external laboratory. For more details refer to section 14 of this report.

17. Evaluation of test results and OOS investigation

The order of investigation and evaluation of results obtained outside the requirements of the specification were described in SOP titled as "Evaluation of results outside the requirements of the specification". A form for the report on the evaluation of results outside the requirements of the specification was required to be completed. A flowchart for evaluation of results beyond the requirements of the specification was included in the applicable SOP.

Analytical test reports were issued by the laboratory based on information recorded in analytical worksheets. The test reports 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

18. Certificate of analysis

The results of each testing were registered in the form of certificates of analysis in the Safety software program. No corrections were permitted in the certificates of analysis.

The certificates of analysis were issued electronically. One copy of the certificates was printed on paper. Upon completion of the data review process, it was the responsibility of the designated person to ensure that the electronic version of the certificate was tamper-proof, and the access was protected by a personal login and password.

The certificate of contained series of information, among others:

- the results of the tests performed with the prescribed limits
- 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.

All test results prior to release were checked by the Head of the TL to ensure accuracy, and only then they were signed by the analysts who conducted the tests, the specialist who accepted the product samples and the laboratory director.

19. Retained samples

Refer to section 14 of this report.

20. Safety

At the time of inspection, staff were observed wearing laboratory coats, appropriate footwear and, suitable eye protection. Special care was taken in handling highly potent, infectious or volatile substances. Highly toxic and/or genotoxic samples were handled in safety cabinets. Safety showers including eye wash statins were installed. Rubber suction bulbs were used on manual pipettes. Safety data sheets were available for all stored chemicals.

Miscellaneous	
Assessment of the Laboratory Information File	The Laboratory Information File in English contained specific and factual information about the operations being carried out at Testing Laboratory and essential steps for each activity were described and where appropriate, supportive documentation was appended. The LIF was submitted for WHO Prequalification.
Annexes attached	N/A

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, ***the Testing Laboratory with the following address*** was considered to be operating at an acceptable level of compliance with WHO GPPQCL Guidelines.

The Testing Laboratory of Territorial Branch of the Republic State Enterprise NCEMMD
9A Bukhar Zhyrau Prospect
Karaganda City
Kraganda Region
Republic of Kazakhstan

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

22. Guidance for organizations performing in vivo bioequivalence studies. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 9.
Short name: WHO BE guidance or ***TRS996 Annex 9***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex09.pdf