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

Part 1	**General information**
Laboratory Details	
Name of the laboratory	Laboratory of Pharmaceutical Analysis, State Expert Centre, Ministry of Health of Ukraine (LPA)
Address of inspected laboratory	14, Antona Tsedika Street (formerly Eugene Pottier Street) Kiev, 03680 Ukraine
GPS Coordinates	Latitude: 50.4611 Longitude: 30.4369
Dates of inspection	11-14 February 2020
Type of inspection	Routine
Introduction	

Brief description of testing activities

Type of analysis	**Finished products**	**Active pharmaceutical ingredients**
Physical/ Chemical analysis	pH, density, refractometry, viscosity, conductivity, water content, acid value, iodine value, peroxide value, ester value, hydroxyl value, saponification value, nitrogen determination, heavy metals, loss on drying, limit tests, disintegration, dissolution, uniformity of dosage units (mass, content), friability, tablet hardness, dimensions	pH, density, refractometry, viscosity, conductivity, melting point, water content, acid value, iodine value, peroxide value, ester value, hydroxyl value, saponification value, acid neutralizing capacity, nitrogen determination, heavy metals, loss on drying, limit tests
Identification	HPLC (UV-Vis, DAD, fluorescence, RI conductive detection), GC, TLC, UV-Vis and basic tests	HPLC (UV-Vis, DAD, fluorescence, RI conductive detection), GC, TLC, UV-Vis and basic tests

	Assay, impurities and related substances	HPLC (UV-Vis, DAD, fluorescence, RI detection), GC, UV-Vis spectrophotometry, AAS, volumetric titrations	HPLC (UV-Vis, DAD, fluorescence, RI detection), GC, UV-Vis spectrophotometry, AAS, volumetric titrations
	Micro-biological tests	Sterility test, microbial limit tests, microbial assay of antibiotics	Sterility test, microbial limit tests, microbial assay of antibiotics
	Bacterial Endotoxin Testing (BET)	Bacterial endotoxins test (LAL)	Bacterial endotoxins test (LAL)
	Stability testing	The Laboratory does not carry out stability testing of medicinal products and does not provide reports or conclusions on stability. However, at the request of the customer, the laboratory conducts quality control of samples' stability results. The list of indicators for quality control of drug samples and the frequency of testing are specified by the customer.	
General information	The Laboratory was founded in 1994 to support the Medicine Registration process in Ukraine as an independent unit of the State Expert Centre amongst other units such as: – Pharmaceutical authorization of products – Design clinical technologies – Pharmacovigilance department – Pharmacovigilance system audit unit – Preclinical and clinical. The objectives of the Laboratory are as follows: – Obtain reliable test results of medicines, – Meeting the needs of customers, – Fulfilment of the tasks assigned by the leadership of PE "State Expert Center"; MoH Ukraine, – Cutting down the cost of analysis,		

	– Reducing the time of analysis to meet the applicable deadlines set up for sample analysis, – Ensuring security at all stages of the analysis and after its completion. An appraisal for quality control analysis of Medicinal Products was issued by the Ukraine State Agency. Additionally, the laboratory was authorized to handle narcotics and psychotropic agents and had the license to work with the agents of groups III-IV of pathogenicity for humans. No substantial changes were implemented since the last WHO inspection in terms of instrumentation, methodologies, activities, facilities and organization. Despite submission of several tender-requests, the laboratory had not received any WHO-prequalified medicinal product - testing assignment. The laboratory statistic showed a reduction in the number of samples received since a legislative amendment (2015) to simplify the medicinal products marketing authorization license registration process.
History	The laboratory was previously inspected by WHO during May 2016.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Quality Management System Personnel Training and Safety Documentation and Records Premises and Equipment Validation – Qualification –Calibration Laboratory Practices Reference standards – Reagents - Water
Restrictions	All QMS related documentation and records were written in local language.
Out of Scope	NIR spectroscopy
Abbreviations	**Meaning**
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
CoA	Certificate of analysis
CAPA	Corrective action & Preventive action
DQ	Design qualification
FPP	Finished pharmaceutical product
FTIR	Fourier transform infrared spectrophotometry or spectrophotometer
GC	Gas chromatography or Gas chromatography equipment

GMP	Good manufacturing practices
HPLC	High-performance liquid chromatography (or high-performance liquid chromatography equipment)
IQ	Installation qualification
IR	Infrared spectrophotometry
KF	Karl Fisher titration
LIMS	Laboratory information management system
MB	Microbiology
MR	Management review
N	Normality
NC	Non-conformity
NCA	National control authority
NCL	National control laboratory
NRA	National regulatory agency
OOS	Out-of-specifications test result
OQ	Operation qualification
Ph.Eur.	European Pharmacopoeia
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PT	Proficiency testing
PTS	Proficiency testing scheme
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QM	Quality manual
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
SOP	Standard operating procedure
TLC	Thin layer chromatography
TOC	Total organic carbon
URS	User requirements specifications
USP	United Stated Pharmacopoeia
UV	Ultraviolet-visible spectrophotometry or spectrophotometer
VMP	Validation master plan
VS	Volumetric solution

Part 2	Summary of findings and recommendations (where applicable)

1. Organization and management

The organization and management structure of the laboratory; including responsibility, authority and interrelationship of the personnel was specified in an organogram. The laboratory consisted of 4 departments, as well as a sector for Quality Assurance, with a total of 28 employees at the time of the inspection:

- Organization Department
- Department of Physical-Chemical methods
- Department of Microbiological Methods and Antibiotics Activity
- Department for Chemical Methods
- Quality Assurance

A local requirement was available to ensure that staff were not subjected to commercial, political, financial and other pressures or conflicts of interest that might adversely affect the quality of their work.

The identified deficiencies related to the organization and management were adequately addressed in the Laboratory's CAPA plan.

2. Quality management system

A quality manual defining the quality management system was available.

The quality policy was provided based on the local legislations and guidelines, ISO/IEC 17025, ISO 9000 series and WHO technical reports.

The Laboratory took part in PT schemes offered by FIP-LMCS (KNMP proficiency programme) and/or WHO on a regular basis. An annual plan for PT was provided. The previous PT results were all verified as satisfactory.

Management review (MR)

SOP for assessment of the functionality of the QA system, effective 2 Jan 2020 was discussed. Management Review was required to take place once a year or more often if needed.

The last performance assessment report, dated Jan 2020 was available.

Samples were required to be tested within 30 days. Although statistics were not provided to quantify whether the target was met, it was claimed that samples were generally tested within the deadline since the volume of testing is proportional to the laboratory's capacity.

Internal audits

The control of internal verification (audits) and corrective actions in the Laboratory were performed by staff who were not involved in the activities in the scope of the respective audit. Audit was conducted according to an approved schedule. Details of internal audit were properly documented as a report, including date of audit, subject of audit, name of audited employee, audit results (if the result was negative comments and recommendations were stated; i.e. revealed nonconformities, proposals for corrective actions) in accordance with SOP for internal audit extended on 19 Jun 2018.

The inspection plan dated 8 Jan 2020 was available. The independency of auditors, as well as their training documentation was verified.

Deviation & CAPA-handling

The handling of deviations and CAPAs was performed in accordance with the respective SOP and it was recorded in a word-document with all necessary information with exception to deadline for closing of the CAPA and the respective classification.

Change control

The changes were classified as (01) organizational, (02) documentation, (03) automated system, (04) methods and calibrations, (05) list of dosage forms, (06) staff, (07) subcontractor, (08) contract laboratory, (09) premises and environmental conditions, (10) customers, (11) suppliers, (12) others in accordance with the applicable SOP.

The cases were identified by a unique code (containing the change type and a serial number) and recorded in an Excel spreadsheet.

Complaints

There was no complaint recorded since the last WHO inspection.

The identified deficiencies related to the QMS were adequately addressed in the respective Laboratory's CAPA plan.

3. Control of documentation

The laboratory had established and maintained procedures to control documents, including preparation, revision, distribution, return and archiving. SOPs were reviewed every three years or more frequent. A master list was available to identify the current version status and distribution of SOPs. SOPs had a unique identifier, version number, date of implementation and reference to the previous version. The documents were released by the QA-Head and available at the relevant location in accordance with a distribution map which was annexed to each SOP.

An SOP was in place comprising the authorization for copying and the identification of copies from official and controlled documents. Relevant staff was trained on new and revised SOPs. The personnel acknowledged by signature that they were aware of applicable changes on a training sheet attached to the original copy of SOP. This training sheet was also used as a training matrix.
The identified deficiencies related to the Control of documentation were adequately addressed in the Laboratory's CAPA plan.

4. Records

Records of analytical tests included calculations, derived data and instrument usage were documented in analytical worksheets which were consecutively numbered. The records were properly archived. Access to the archive-cupboard was restricted only to the authorized personnel.

The identified deficiencies related to the Records were adequately addressed in the Laboratory's CAPA plan.

5. Data processing equipment

An inventory of all computerised systems was available with information about their unique identification, purpose, validation status, physical or storage location of the software (drive and files path) and responsible or contact person.

Electronic data was protected from unauthorized access and backed up at appropriate regular intervals in accordance with SOP for laboratory data – information management system, dated 20 Jan 2020. The operating system-level access control of the computerized systems was managed by the IT staff of the Expert Centre in accordance with the applicable SOP.

Data was recorded on a storage device by the analyst at the end of each project, handed over to QA-head who was then transferring data to a folder located on a server managed by the IT of State Expert Centre, located in another building. The access to the folders were restricted to the QA and laboratory director. IT-department was responsible for back-up and computerized systems. During the internal audit, a restoration of data was carried out to verify the integrity of the data stored on the server.

Concerning spreadsheets (e.g. Excel®), the laboratory was not using any validated Excel spreadsheet. The Excel spreadsheets were used to calculate the results; however, the calculations were verified by using a calculator and confirmed by QA-Head or her designee.

The chromatography software system was upgraded on 18 Oct 2019 based on an agreement in which the expectations, including the general functionality, audit trail and access rights were outlined. Documentation for IQ and OQ validation of the new software system was provided by the supplier.

The identified deficiencies related to the Computerized systems were adequately addressed in the Laboratory's CAPA plan.

6. Personnel

The laboratory had sufficient personnel with the necessary education, training, technical knowledge and experiences for their assigned functions. Staff undergoing training was assessed on completion of the training and added to the competency matrix which was provided as a controlled documentation. The list was revised as soon as an employee was assigned to new activities.

The Laboratory maintained current job descriptions for all personnel involved in tests and/or calibrations. The laboratory maintained also records of all technical personnel, describing their qualifications, training and experience.

Job descriptions, training documentation and CV of randomly selected staff were reviewed.

7. Premises

The layout of the laboratory premises was described in a document.

The Laboratory premises (including offices, Physico-Chemical Laboratory, Chemical Laboratory, Microbiology Laboratory, Sample reception and storage, Toiletry, Dining room) were of suitable size and design to suit the functions and to perform the operations to be conducted in them. Sample storage on ambient, 2-8°C and frozen -20°C was assured. Access to the laboratory facilities was restricted to designated personnel.

Different premises, rooms and cubicles of the Microbiology Laboratory were appropriate for working with sterile and non-sterile samples and safe-handling of microorganisms. The critical areas of the microbiology laboratory premises were classified, controlled and qualified. The construction, qualification and monitoring of aseptic laboratory rooms were discussed. SOP for Ventilation systems in the working room of microbiological control of the HVAC system was available.

The qualification of the class "B" room was carried out annually covering non-viable particles, air change, filter integrity, pressure differences and air change in accordance with the EU GMP Annex 1 requirements. Specification of the rooms were defined in SOP for perform of qualification of clean room premises and HVAC system, extended on 13 Nov 2019. Acceptable ranges were defined in the SOP.

Maintenance of air-conditioning system and monitoring of clean rooms were performed quarterly according to a contract.

There was a biosafety box, Class II located in the sterility room providing aseptic conditions and for additional protection of the operator environment. SOP for its qualification was revised on 13 Nov 2019. The records of the recent qualification (as due once in every 6 months, dated on 11 Nov 2019) were available.

The identified deficiencies related to the Premises were adequately addressed in the Laboratory's CAPA plan.

8. Equipment, instrument and other devices

The equipment, instruments and other devices used for the performance of tests, calibrations, validations and verifications were required to undergo a successful calibration/validation/qualification procedure before being approved for usage according to the general policy, dated 01 Jul 2019. The list of the equipment together with the main qualification, calibration and maintenance data was provided as an Excel spreadsheet with restricted access.

Several equipment and/or related qualification documentation available were reviewed to verify the adequacy of their calibration/validation certificates.

The identified deficiencies related to the Equipment and other devices were adequately addressed in the Laboratory's CAPA plan.

9. Contracts

The laboratory had not subcontracted any testing at the time of inspection.

Suppliers and service providers were evaluated, listed and qualified by the laboratory Head in accordance with the applicable SOP.

The evaluation records of the supplier for Millipore water generator consumables were discussed.

10. Reagents

The reagents and prepared reagent solutions were of appropriate quality and correctly labelled and stored. The preparation of the reagent and volumetric solutions was recorded with information about name, date of preparation, initials of technician or analyst, expiry date/retest date, concentration, molarity and standardization factor, as applicable.

The quality of water was regularly verified to ensure that the various grades of water met the appropriate specifications in accordance with applicable SOPs and local monographs. Tests include off-line conductivity, and microbiology.

Laboratory used solid and liquid culture media manufactured by Merck (Germany) and BioMerieux (France) according to National Pharmacopoeia of Ukraine, European Pharmacopoeia, British Pharmacopoeia and Pharmacopoeia of United States. Each obtained batch of culture medium had a certificate of quality. Each prepared batch of medium was tested for sterility, growth, indicative, selective and inhibitory properties and recorded on a form for "Growth inhibition of Growth Media". SOP for verification of the growth inhibition and indicative properties of the growth media used to test non-sterile MP for Micro count or purity, identification of some MO, extended 20 Jun 2018 was available. There was an Excel sheet with an inventory of Growth Media used in the laboratory, with information regarding the code, internal assigned number and received. This inventory was also used for reconciliation purposes.

Detergent specification used for dishwashing machine was defined and the respective certificate of analysis was provided.

The identified deficiencies related to the Reagents were adequately addressed in the Laboratory's CAPA plan.

11. Reference substances and reference materials

Reference materials used for testing were provided by the customer and accompanied the test sample. The reference materials were stored in a dedicated place in the sample storage room. The Usage was recorded in the test records. Following to the accomplishment of the test, the respective reference standard was returned to the customer together with the Certificate of Analysis.

Official, pharmacopeial standards were used for qualification of equipment. The following information was kept on the labels of reference substances and/or the accompanying documentation (as appropriate): name and description of the material, batch or control/identification number, source, date of receipt or preparation , use of the reference substance, expiry date or retest date, location of storage and storage conditions, certificate/batch validity statement of compendial reference substances, testing results (CoA) and assigned content, together with the safety data sheets. The identification number was quoted on the analytical worksheets whenever the reference substance was used. When pharmacopeial standards were used, the batch validity statement was attached to the analytical worksheet.

A register for all reference substances was also available in an Excel spreadsheet. Dispensing of the Reference standards were recorded in a template with all required information.

Reference cultures were provided for establishing acceptable performance of media, for validation of methods, for verifying the suitability of test methods and for assessment or evaluation of ongoing performance. The reference cultures were provided from National Academy of sciences of Ukraine – Zabolotny institute of microbiology and virology in lyophilized condition. Reference cultures were subcultured once to provide reference stocks, parallel with execution of purity and biochemical check. Working cultures for routine use were primary subcultures from the reference stock. Up to five generations could be subcultured from the original reference strain as per the applicable SOP.

The identified deficiencies related to the Reference materials were adequately addressed in the Laboratory's CAPA plan.

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 and regularly using suitable test weights. Requalification was performed annually using certified reference weights.

Records/logbooks were kept for items of equipment with information to identify the device, current location, maintenance carried out, history of damage, malfunction and modification or repair.

The laboratory Equipment Master Plan provided an overview of the qualification/calibration /validation approach of equipment and computerized systems.

For more details refer to section 8 of this report.

13. Traceability

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

The devices used for verification were all traceable to SI unit, noted on the documentation.

The identified deficiencies related to the Traceability were adequately addressed in the Laboratory's CAPA plan.

14. Incoming samples

The laboratory was not involved in sampling process. Samples were received from:

- Expert Centre for Marketing Authorization – Preauthorization control
- Manufactures to test the stability and QC (already registered products – post marketing purposes)
- APIs, based on the manufacturer's requests. In accordance with the local law, API was not required to be tested by the authority.

The samples were received from the customer together with the accompanying documentation; including QC method, reference material, columns, as applicable.

The test request accompanied each sample submitted to the laboratory contained amongst the following information:

- Name and batch number of the sample
- Specification and test methods to be used for testing
- Required storage conditions
- Name of the applicant and the manufacturer (if different)

All samples were assigned a registration number by the officer of the Logistic Department responsible for receipt and handling in accordance with the applicable SOP. A paper-based register (logbook) was kept.

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

The samples either due for testing or archived (retention samples) were placed in the storage room under defined storage conditions. Retention samples were stored for 6 months.

The identified deficiencies related to the Incoming samples were adequately addressed in the respective Laboratory's CAPA plan.

15. Analytical worksheet

The analysts recorded information about samples, test procedures, calculations and results in analytical worksheets, which were completed by raw data. All values obtained from each test, including blank results, were immediately entered on the analytical worksheet and all graphical data, either obtained from recording instruments or plotted by hand, were attached or were traceable to the electronic record file and/or document where the data was available. Analytical worksheets from different departments related to the same sample were assembled together.

The worksheets contained the following information:

- The date on which the analysis was started and completed
- Reference to specifications and 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
- The conclusion whether the sample was found to comply with the specifications
- Deviation from the prescribed procedures

The completed analytical worksheets were signed by the responsible analyst and verified, approved and signed by the supervisor and QA-Head.

The identified deficiencies related to the Analytical worksheet were adequately addressed in the Laboratory's CAPA plan.

16. Validation of analytical procedures

The chemical and physicochemical test methods were received from the customer and considered as validated and directly applicable without further method transfer confirmation or even verification. For chromatography methods, the system suitability was implemented.

The laboratory carried out validation procedures of sterility testing (according to 2.6.1 EP), microbiological examination of non-sterile products (according to 2.6.12 EP 2.6.13 EP and 2.6.31 EP), and validation characteristic of microbiological assay of antibiotics (trueness, repeatability, linearity and interlaboratory accuracy).

The identified deficiencies related to the Validation and verification were adequately addressed in the Laboratory's CAPA plan.

17. Testing

Tests were recorded in pre-printed analytical worksheets.

It was stated in the applicable SOP that the setup of the integration parameters and the integration of the chromatograms would happen following to the completion of the injection of the whole sequence (including blank, system suitability, standards, samples, bracketing standards, as applicable). The laboratory was aware that the same integration parameters should be used throughout the analytical run.

Test records were randomly selected and reviewed.

Assay of microbiological tests were accompanied by the conforming checks, i.e. the check of suitability of procedures with utilization of the conforming tests - strains; the check of sterility of culture media, the solvents, washing fluids, systems of membranous filtration, the check of sterility, growth, indicative, selective and inhibitory properties of media, the check of an aseptic conditions of assay, the check of regimes of determination, the check of a state of clean premises and requirements of an external environment.

SOP for LAL testing, SOP for confirmation of the declared sensitivity for the LAL test reagents and SOP for sequence to perform the stages of testing of the parameter LAL with the method suitability verification were available and reviewed to ensure that clear procedures were provided.

The identified deficiencies related to the Testing were adequately addressed in the Laboratory's CAPA plan.

18. Evaluation of test results and OOS investigation

The analytical records prepared by the different departments were collected and recorded in a logbook before they were transferred to the QA.

Data were reviewed by QA in accordance with the applicable SOP and the respective checklist.

An SOP was in place describing the investigation process of OOS test results. When a doubtful result (suspected OOS result) was identified, a review of the procedures applied during the testing process was undertaken by the supervisor and the analyst. The SOP gave guidance on the retesting including to repeat of tests by a second experienced and competent analyst.

The OOS investigation records of randomly selected sample were reviewed and discussed.

The laboratory had not reported any invalidated OOS result in the recent years. Invalidated OOS were recorded in the same logbook used for documentation of OOS incidents.

19. Certificate of analysis

After the QA review of the analytical worksheets, a document titled as "Conclusion about quality" based on the test request documents, test results and the specification were created. The main content of the certificate was in accordance with the applicable requirements such as:

- Sample name, batch number, expiry date
- Sample internal (Laboratory) code
- Customer name
- Request receipt date
- Reference to the test methods and quality specification
- Signature of the laboratory head
- Issue date

The document was presented in a letter with the Laboratory of Pharmaceutical Analysis logo in three (in case of preauthorization) and two (in case of post authorization) original copies. One copy was mailed to the Customer, the other was archived in the Laboratory and the third one was submitted to the Centre (as applicable).

20. Retained samples

The Logistic staff was responsible for the sample receipt and management, and calculation of the theoretical amount of the sample required for testing and retention.

Retained samples were kept in their final pack and archived for 6 months in the sample room under controlled temperature (ambient, 2-8 ^{0}C or frozen, as applicable).

21. Safety

Staff was wearing laboratory coats, including eye protection with the same dress code applicable to visitors. Special care was taken in handling of highly potent, infectious or volatile substances. Highly toxic and/or genotoxic samples/reagents were handled in safety cabinets. Safety showers were installed. Rubber suction bulbs were used on manual pipettes. Safety data sheets were available before testing was carried out. First aid kits were provided and kept up-to-date for every departments.

The regular and documented training of the safety instructions covered amongst high voltage electrical safety, first aid, electrical devices, operations at the chemical laboratory, preparation of disinfectants, pressurized containers, autoclaves, handling of acids, alkaline and other active substances, organic solvents, narcotics, psychotropic agents and precursors, centrifuges, germicide lamps and heavy load.

Miscellaneous	
Assessment of the Laboratory Information File	Laboratory's Information File (LIF) was provided in English. The document was revised to reflect the current situation.
Annexes attached	N/A

Part 3 – Conclusion – Inspection outcome

Based on the areas inspected, the people met, and the documents reviewed, including the CAPA plan provided for the observations listed in the Inspection Report, ***Laboratory of Pharmaceutical Analysis, State Expert Centre, Ministry of Health of Ukraine (LPA)***, located at ***14, Antona Tsedika St., Kyiv, 03057; Ukraine*** is 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 Laboratory, to a satisfactory level, prior to the publication of the WHOPIR.

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

Part 4	List of WHO Guidelines referenced in the inspection report

1. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 1.
   Short name: WHO GPPQCL Guidelines or ***TRS No. 957, Annex 1***
   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

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