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Prequalification Unit Inspection Services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Quality Control Laboratory

Part 1	**General information**
Inspected laboratory details	
Name of Laboratory	Prime Health Pvt Ltd
Address of inspected laboratory site	79-C, Al-Murtaza Commercial, Lane 2, Phase VIII , DHA, Postal Code 75500, Karachi, Pakistan
Inspection details	
Dates of inspection	9 – 10 September 2024
Type of inspection	Routine inspection
Inspection record number	INSP-QCL-2020-0048
Introduction	
Brief description of testing activities	

Type of Analysis	Finished Products	Active Pharmaceutical Ingredients
Physical/Chemical analysis	pH, Water content (Karl-Fisher), loss on drying, dissolution, uniformity of dosage units, titration, polarimetry	pH, Water content (Karl-Fisher), loss on drying, dissolution, uniformity of dosage units, titration, polarimetry
Identification tests	HPLC, UV-VIS Spectrophotometer, FTIR	HPLC, UV-VIS Spectrophotometer, FTIR
Assay, impurities and related substances	HPLC (UV-VIS, DAD, RI detection), UV-VIS Spectrophotometer, Determination of related substances and impurities by comparison with reference standards, polarimetry	HPLC (UV-VIS, DAD, RI detection), UV-VIS Spectrophotometer, Determination of related substances and impurities by comparison with reference standards, polarimetry
Stability studies	ICH conditions	ICH conditions
Microbiological analysis	Not applicable	Not applicable
Miscellaneous	Not applicable	Not applicable

General information about the laboratory	Prime Health (Pvt) Ltd (in short PHPL) is Pakistan's first laboratory to offer customer-specific contract pharmaceutical analytical services (drug substances and drug products). PHPL has an area of approximately 8,256 square feet. Services offered by PHPL include pharmaceutical equivalence studies (comparative dissolution profiling), stability testing, raw materials

	testing, finished pharmaceutical products testing, analytical method development and validation/verification of analytical methods. The laboratory activities were relocated from Islamabad to Karachi in 2022/2023 while no change was introduced to the laboratory management, policies, regulations and quality management system.
History	The initial inspection of the site based in Islamabad belonging to Prime Health Pvt Ltd was conducted from 22 to 24 January 2020 (inspection record: INSP-2018-02225). The testing activities of this quality control laboratory was relocated from Islamabad to Karachi in 2022/2023, while maintaining the same QMS.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	The scope of the inspection was limited to the activities of the physico-chemical testing. The inspection covered all sections of the WHO Good Practices for Pharmaceutical Quality Control Laboratories (GPPQCL) namely: 1. Organization and Management 2. Quality management system 3. Control of documentation 4. Records 5. Data processing equipment 6. Personnel 7. Premises 8. Equipment, instruments and other devices 9. Contracts 10. Reagents 11. Reference substances and reference materials 12. Calibration, verification of performance and qualification of equipment, instruments and other devices 13. Traceability 14. Incoming samples 15. Analytical worksheet 16. Validation of analytical procedures 17. Testing 18. Evaluation of test results 19. Certificate of analysis 20. Retained samples 21. Safety
Restrictions	N/A
Out of scope	The laboratory had facilities for microbiological testing; however, these were not covered during the WHO inspection since these testing activities were out of the scope of the designated WHO prequalification of PHPL.
Abbreviations	**Meaning**
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
CoA	Certificate of analysis
FPP	Finished pharmaceutical product
FTIR	Fourier transform infrared spectrophotometry or spectrophotometer

GC	Gas chromatography or Gas chromatography equipment
GMP	Good manufacturing practices
HPLC	High-performance liquid chromatography (or high-performance liquid chromatography equipment)
KF	Karl Fisher titration
LIMS	Laboratory information management system
MB	Microbiology
MR	Management review
NC	Non-conformity
NCA	National control authority
NCL	National control laboratory
NRA	National regulatory agency
OOS	Out-of-specifications test result
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometry or spectrophotometer

Part 2	**Summary of the findings and comments**

1. Organization and Management

Prime Health Private Limited had defined the organisation and management structure, responsibilities, authority and interrelationship of personnel in the organisational chart. The "General Manager Operations" was in charge of the laboratory and responsible for overall direction and activities of the laboratory. The Quality assurance function was established as an independent function, and led by the Lead QA, Manager.

The Laboratory had arrangements to ensure that its management and personnel were not subjected to commercial, political, financial and other pressures or conflict of interest that might adversely affect the quality of their work. Conflict of interest was managed by signing a designated form by all technical personnel. Additionally, the laboratory had a policy in place to ensure the confidentiality of information included in test reports. Confidentiality was managed through requiring staff to sign the confidentiality code of conduct.

The Laboratory had previously been pre-qualified by WHO at its previous location in Islamabad, Pakistan. Additionally, the following certifications were in place: ISO-9001:2015 Quality management system, certification number 17760-Q15-001, and Lab accreditation ISO/IEC 17025:2017 by Pakistan National Accreditation Council (PNAC), accreditation number LAB 184.

2. Quality management system

The laboratory established, implemented and maintained a quality management system according to ISO 17025 and WHO TRS for GPPQCL. A quality manual was available, and it described the policies, systems, programs, procedures and instructions for the laboratory QMS.

Management review meetings were described in the procedure for management review. MRMs were conducted on a bi-annual basis and were attended by all departmental Heads, including the Manager QC, QA Lead, Manager HR and Administration, General Manager and Manager IT. A generic meeting agenda was described as part of the SOP and included a review of several QMS elements.

Records related to the last two previous meetings were reviewed. Attendance records and action points with responsibilities and timelines were in place. The minutes included a discussion of various QMS elements.

SOP for quality objectives was in place. Quality objectives were developed each year and monitored to ensure their implementation throughout the year.

Change Control Management

Change management was described in a well-established procedure. The procedure described the initiation, review, execution, approval and implementation of changes at the facility related to equipment, processes, procedures and facilities. Changes were classified as major, minor (based on the potential or real impact on the quality attributes of process parameters equipment and validated state of any process or lab activity), and further as temporary or permanent. Departmental Heads were in charge of performing assessments for all changes and listing required actions. Head QA was in charge of reviewing all documentation related to changes prior to final approval by the "General Manager Operations". Post-effectiveness checks and risk assessments were performed as part of the change management process.

A change control logbook was in place and listed the various changes implemented at the facility.

The change record registered in 2022, *CC/001/2022,* regarding the relocation of Prime Health Private Limited from Islamabad to Karachi was selected for review. The reason for the proposed change was presented as a business case. Impact assessments, action points and Quality risk assessment were conducted as part of the change.

Complaints management.

The SOP for customer complaints and feedback was in place and described the collection, receiving, processing, evaluation, responding and handling of all reported customer complaints. QA department was in charge of coordinating the investigation and assigning the responsible team, according to the investigation form. CAPA were applied after the completion of the investigation of the complaint. Customer feedback was managed through the same process, a logbook was in place, and feedback

related to each process was documented. A scoring system was requested based on service-related questions. A score below 20 out of 40 marks would mandate an improvement action.

Out of Specification results.

Handling of Out of Specification Test Results was described in the respective procedure. The approach included a three-phase investigation; 1A, 1B, II and III. A checklist was used for the initial investigation under phase 1A for laboratory errors and another checklist was used in the phase 1B investigation. Initial and extended hypothesis testing was described following an experimental plan or protocol. Provisions of the SOP described the involvement of the manufacturer through notification of OOS results for phase II investigations. A timeline of 45 days was stipulated for the management of OOS results, with the possibility of further extension to 75 days. Quarterly trending of OOS results was also described.

An OOS logbook was in place. Confirmed OOS results were communicated to the customers. Records related to a couple of OOS results were reviewed and discussed.

3. Control of documentation

The SOP for management of document control was in place. The SOP provided guidance on document hierarchy, good documentation practices, initiation of documents, document number identification, creation of documents including format and content, authentication and approval of documents, scanning and storage of documents, distribution, revision and cancellation of the documents. In terms of hierarchy, 4 levels of documents were considered namely level 1: policies and manuals; level 2: quality system procedures and technical procedures; level 3: standard operating procedures (SOPs), standard testing procedures (STPs) and work instructions (WIs); and level 4: forms and checklists. In terms of document number identification, the format of the document number was <Department>/<Document Type>/<Document Title>/<Number>. The review period of the documents was set at once every 3 years or earlier as necessary.

The list of SOPs was provided to the inspectors, and a number of the SOPs were spot-checked during the course of the inspection.

4. Records

Records were kept in hard/paper copies at PHPL for 10 years in the document retention room on the third floor.

An SOP for data integrity was in place at PHPL. It provided guidance on data generation, retention, and monitoring in accordance with ALCOA principles, including the use of audit trails.

The records of any particular test comprised mainly the request for quotation, the request for analysis which accompanied the samples provided by the customer, sample receiving inspection checklist, sample registration including assigned sample ID, issue of sample from QA to QC, analytical worksheet, review checklist/compliance form and the certificate of analysis. The records of testing of a number of product batches were spot-checked.

5. Data processing equipment

The SOP for control of chromatographic integration was in place. The SOP provided comprehensive guidance on peak integration (whether automatic or manual) using HPLC with several examples of scenarios in which manual integration may be allowed, including peak splitting, adding area due to a co-eluting interferant, failure to detect a peak, excessive peak tailing due to a failure of the instrument response to return to baseline or a rise in the baseline and failure to separate peaks. It was evident that the analyst was not allowed to perform manual integration due to lack of rights and privileges in the HPLC software. Rather, the QC Manager had the right to perform manual integration of HPLC peaks when necessary. The audit trail was used as a tool to check if manual integration was considered or not. In addition, the SOP for good chromatographic practices guided, among others, the data processing and management from laboratory equipment, particularly with respect to the audit trail. The audit trail checklists for HPLC and UV spectrophotometer were spot-checked.

In terms of computerized systems, PHPL had a procedure for computerized system validation which briefly described software validation covering the process from URS through to IQ, OQ and PQ. The SOP also briefly described regular review of computerized systems, including review of performance, changes, deviations, problems, software upgrade, audit trail, among others.

The software use policy was in place. The policy included guidance on user's access and authorization matrix. Similarly, SOP for data backups and recovery was followed. The SOP included a figure representing the IT network and infrastructure. The frequency of data backup was set for daily on local machines, monthly and quarterly on local servers and monthly on cloud servers. No laboratory information management system (LIMS) was utilized at PHPL.

6. Personnel

The laboratory had sufficient personnel with the necessary education, training, technical knowledge and experience for their assigned functions. A list of key personnel updated by HR revealed a total of 18 staff, these were observed to have various educational qualifications such as pharmacy, chemistry, engineering, microbiology and science degrees. Staff experiences were varied and generally reasonable.

Job descriptions for the General Manager Operations, Laboratory Attendant, Lead QA Manager and Manager Quality Control were selected for review. The job descriptions were observed to be signed by the job holders.

Personnel were trained in accordance with the training procedure. Training encompassed orientation, work-specific area training, on-the-job training, skills development training, technical training, and training on procedures. The responsibility for training needs identification was the role of departmental managers. The QA manager was responsible for preparing the annual training schedule in consultation with HR and departmental heads. The training schedule was approved by the General Manager Operations. The effectiveness of training was assessed using various assessment tools, included written evaluations, observation of procedure, process and outcome, response to oral queries, testing of blind QC samples and testing of known samples. Re-trainings were required in case of any change, unsatisfactory performance or failure of assessment. The procedure further described the requirements for trainers, including subject matter expertise, technical, social and communication skills.

The following records related to trainings were discussed:

- Training schedule for 2024. The training topics included data integrity and ALCOA, quality risk management, handling and working on gas chromatography, method validation, verification and transfer of methods, computerised data and information security, deviation management procedure, among others.
- Data integrity training
- Handling and storage of laboratory chemical reagents. Training effectiveness was done through scoring of parameters, introduction to the topic, understanding of the topic, knowledge improvement after training, interaction level in this training program and overall effectiveness.

7. Premises

PHPL premises covered an area of approximately 8,256 square feet. The premises were located on a storied building with four floors.

- The first floor housed the admin section, inclusive of a reception area, management office, conference, cafeteria and restrooms.
- The second floor housed the instrument laboratory, inclusive of the stability room, GC and AA room, instrument room, and retention room.
- The third floor housed the chemical laboratory, inclusive of the balance room, chemical storage area, records room and QA offices.
- The fourth floor housed the microbiology laboratory (this laboratory was not subject to the WHO inspection as it is not included within the scope of prequalification).

Generally, the laboratory facilities were of suitable size, design, construction and location. The facilities were clean, tidy and well organised. Access to the testing and storage areas was restricted and only accessible through biometric electronic access by authorised persons. It was observed that the sample retention and storage areas were under the authority of QA and access-controlled.

Separate storage facilities were maintained for the secure storage of samples, retained samples, reagents, laboratory accessories and reference substances. Where necessary, cold storage facilities, refrigeration (2-8^{0}C) and frozen (-20^{0}C), were utilised.

Thermo-hygrometers were in place to monitor the environmental conditions of the laboratory, i.e., temperature and humidity.

8. Equipment, instruments and other devices

In general, the equipment at PHPL was adequately designed, properly located, calibrated, qualified, verified and maintained. Equipment was purchased from suppliers who were capable of providing full technical support and maintenance. The process of purchase and maintenance of purchased equipment, in coordination with the supplier, was well established as per the SOP for handling, calibration and management of laboratory equipment. The master list of laboratory instruments was checked.

The SOP for preventive maintenance of equipment was in place. The preventive maintenance plan of the premises for Q3/2024 was spot-checked. The daily, weekly and monthly verifications/checks of the equipment using template for equipment preventive maintenance plan were also verified. The schedule for preventive maintenance was spot-checked.

9. Contracts

The procedure for selection and qualification of contractors was in place. The procedure was applicable to contractors providing technical services related to testing at the laboratory. The procedure involved the initial filling of the selection and qualification of contracted service provider form followed by a desktop audit of suppliers by QA.

The procedure described the various categories of certifications required for various suppliers. Suppliers were qualified for 3 years and were re-evaluated thereafter. A scoring system based on several parameters was implemented for suppliers. Suppliers scoring below 50 percent were disqualified.

10. Reagents

The laboratory reagents were purchased according to the SOP for purchase policy. The SOP for handling and storage of laboratory chemicals and reagents was in place for procurement, receipt, identification, labelling, validity, storage and disposal of materials including reagents and chemicals. The list of qualified contractors was provided and the evaluation performed of one provider of reagent chemicals using the template for selection and qualification of the contracted service provider as well as the contract service agreement were spot-checked.

The SOP for laboratory solution preparation, factorization and shelf-life determination was in place. The SOP guided the solutions preparation including working with solvents, working with solids, factorization of volumetric solution and shelf-life determination of the prepared solution. During the laboratory tour, it was observed that prepared solutions were properly labelled, stored and well managed.

11. Reference substances and reference materials

The SOP for the management of reference standards was in place. The SOP provided for the inventory control, purchase/procurement, receipt, storage, qualification and handling/use of reference standards as well as preparation of reference standard solutions prior to use. The SOP also guided the development of secondary/working standards. Reference and working standards were securely kept in a cabinet located on the third floor of the laboratory. Analysts' access to the cabinet of the reference and working standards was limited. Logbooks, established for reference, and working standards were available. The list of standards was also verified.

For LC and GC, the SOP for management of columns was in place. The SOP guided the process of checking new columns, usage of GC columns, column conditioning of GC and HPLC columns, performance checks of columns, column usage, column regeneration, and discarding/withdrawing of the columns.

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

SOP for handling, calibration and management of laboratory equipment was in place. The SOP provided general guidance on procurement of laboratory equipment, receipt, storage, and installation of equipment, safe handling of equipment, transport of equipment, equipment records, operating instructions, instrument calibration and maintenance system, and repairing of equipment. Specific calibration and verification requirements for specific equipment (e.g., weighting balances, and

pH meters) were provided in the respective work instructions. Examples of the latter, namely work instructions for semi-micro analytical balance and work instructions for pH meter were spot-checked.

The laboratory instruments calibration program was checked. The frequency for calibration of laboratory instruments was not established in a policy or procedure document. Rather, the frequency was included within the laboratory instruments calibration program, which was annexed as a template to the SOP for handling, calibration and management of laboratory equipment.

The daily verification was spot-checked for the weighing balance at the wet chemistry laboratory on the third floor of PHPL. The calibration atomic absorption spectrometer, gas chromatography, HPLC, and UV/VIS spectrophotometer were spot-checked.

In addition, the master validation plan was in place. The VMP guided the qualification / re-qualification of the instruments/equipment at PHPL, including the user requirement specifications (URS), IQ, OQ, and PQ along with the relevant documentation and the review, approval and execution of the annual plan for qualification/validation. The 2023 master validation plan was checked, and it reflected that all equipment qualification and temperature mapping were completed between January and March 2023. The 2024 master validation plan was checked.

SOP for instrument qualification was in place. The SOP provided comprehensive guidance on qualification activities, starting with URS, through to IQ, OQ and PQ. A template for the periodic laboratory instrument qualification program was annexed to the SOP and was spot-checked. A policy was in place for requalification of all equipment every 5 years, if not earlier, due to change control aspects.

When instruments equipment did not satisfy the calibration or qualification criteria, the SOP for non-conforming instruments/equipment was followed. The relevant process included proper labelling of the instrument as “out of order”, notification of the responsible staff followed by the necessary intervention (e.g., maintenance and repair) along with documentation of the same in terms of an “instrument breakdown report”.

13. Traceability

The SOP for measurement traceability was in place. The SOP provided for traceability of measurements to established standards (e.g., international standards [SI] whenever available and possible. Alternatives to SI included certified reference materials provided by competent suppliers, use of specified methods and consensus standards that are clearly described and agreed by the relevant parties. The SOP also provided guidance on SI and other standards.

14. Incoming samples

Samples were received from various clients, mainly pharmaceutical manufacturers. A test request accompanied each sample submitted to the laboratory and contained information on the source of each sample, description of the sample, specification to be used for testing, and other relevant information. The laboratory provided a quotation to the client that included the inputs/resources required for testing, including the number of samples required.

Received samples were divided into two portions, one portion for submission to the laboratory for immediate testing, while the second portion was kept for retention purposes.

Laboratory sample management was described in the respective SOP. Samples were checked and visually inspected at receipt according to a checklist. Samples were coded and labels attached prior to transfer to the storage areas awaiting testing.

15. Analytical worksheet

Analytical worksheet templates were available for each product being tested. These were controlled and issued by the QA unit. Information on samples, test procedures, calculations and results were recorded in the respective fields within the analytical worksheets.

All values obtained from each test were required to be immediately entered on the worksheet and all graphical/numerical data obtained from recording instruments were attached or traceable to the electronic record file.

The completed analytical worksheets were signed by the responsible analyst and verified, approved and signed by the supervisor. The analytical worksheet for few samples was spot-checked.

16. Validation of analytical procedures

The analytical method validation (AMV) was guided by several documents, including mainly the SOP for analytical test method verification and validation. The SOP provided guidance on validation of non-pharmacopeial test methods and verification of pharmacopeial methods, as well as validation of modified methods, revalidation and method transfer. The SOP comprehensively provided guidance on the documentation of AMV in terms of validation protocols and reports. For the purpose of risk categorization of AMV, the SOP described five categories of analytical methods namely:

- Category I: quantitative assessment of major components (i.e., assay, content uniformity, determinative step for dissolution/release rate). The required validation parameters included system suitability, accuracy, precision, linearity and specificity.
- Category IIa: quantitative assessment of minor components (i.e., impurity and detergent quantitative determinations). The required validation parameters included system suitability, accuracy, precision, linearity and specificity and limit of quantitation.
- Category IIb: qualitative assessment of minor components (i.e., impurity and detergent limit tests). The required validation parameters included specificity and limit of detection.
- Category III: performance tests components (i.e., dissolution, drug release, particle size). The required validation parameters included precision, all other parameters based on the nature of the specified test.
- Category IV: identification tests. Required parameter was specificity.

The SOP also provided guiding ranges of the different AMV parameters. The SOP referenced ICH Q2/R1, WHO guidelines on validation, USP <1225> and USP <1226>. In total, PHPL validated 27 test methods, apart from verified pharmacopeial test methods. The list of the validated test methods was provided and sample validations were spot-checked.

The analytical method verification protocols and reports of assay of a couple of products were reviewed.

17. Testing

Test procedures were described in detail and allowed analysts to perform the analysis in a reliable manner. Products were either tested according to pharmacopeial specifications or customers' methods. Pharmacopeial methods were verified prior to use in testing, while in-house methods were validated before use.

18. Evaluation of test results

The SOP for non-conforming tests and work was in place. The SOP guided the reporting of non-conforming tests and work using the prescribed template, followed by the assignment of a responsible person to undertake the investigation as per the respective procedure. If an assignable root cause was identified, corrective and preventive actions were considered.

The measurement uncertainty was estimated through a number of approaches and practices at PHPL, including regular participation in the proficiency testing scheme. The SOP for proficiency testing (PT)/inter-laboratory comparison program was in place. The SOP provided guidance on participation in proficiency testing schemes, covering the entire process from identifying and applying to relevant PT schemes, through sample receipt, handling, and testing, to reporting and evaluation of PT results. The SOP mandated the participation of PHPL in at least one PT activity in each sub-discipline within the laboratory's scope per year. In 2023, PHPL participated in 23 PT activities. In 2024, PHPL participated in 19 PT activities. The summary of the PT results was available at PHPL and was among the subjects discussed during the management review meetings.

19. Certificate of analysis

The SOP for result reporting was in place. The SOP provided for compilation of test results after testing, reporting of figures including rounding off, entry of results into the database, review process, generation of the CoA, reporting statement of conformity and format of the COA. The final review checklist annexed to the SOP for result reporting was not comprehensive as some key check activities were not considered (e.g., audit trail).

A certificate of analysis was prepared for each sample/batch of product and contained a series of information depending on the sample analysis requisition, including

- the results of the tests performed within the specified limits.
- a conclusion as to whether the sample was found to be within the limits of the specification.
- the analytical test methods.
- the date on which the test results were completed.

20. Retained samples

A documented retention sample management procedure was in place. A dedicated area for the storage of retained samples was established on the second floor. Access to this area was restricted to authorized persons (in this case, staff of the QA unit). Samples were stored on mobile racks on labelled shelves and their respective location were tracked. Shelves were segregated as quarantine, pretest samples and tested samples. Sample quantities were selected to allow two re-analyses. Retention samples were kept for one year after expiry.

Monitoring and recording of environmental conditions were performed as per the respective SOP. Environmental monitoring data was recorded in centralized environmental monitoring devices, and these were reviewed on a bimonthly basis.

21. Safety

Safety precautions were generally implemented at the laboratory. Staff were wearing laboratory coats, including eye goggles were required. Safety cabinets were installed for handling highly volatile, potent or toxic samples. Eye showers were installed in easily accessible points within the laboratory. Rubber suction bulbs were available for use with manual pipettes. Safety data sheets for various materials were available and spot-checked.

SOP for storage and handling of gas cylinders was in place, and described the receipt, checks and storage of gas cylinders used in the laboratory. Safety precautions were sufficiently described in the SOP.

Part 3	Conclusion – Inspection outcome

Based on the areas inspected, the people met and interviewed, and the documents reviewed, and considering the findings of the inspection including the observations listed in the Inspection Report, **Prime Health (Pvt) Ltd**, located at **79-C Al-Murtaza Commercial, Lane 2, Phase VIII-A, DHA, Karachi – 75500, Pakistan**, was considered to be operating at an acceptable level of compliance with WHO Good Practices for Pharmaceutical Quality Control Laboratories (GPPQCL) Guidelines.

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

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

Part 4	List of WHO Guidelines referenced in the inspection report

1. WHO good 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
   https://www.who.int/publications/m/item/trs986-annex2

2. 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
   https://www.who.int/publications/m/item/annex-2-trs-957

3. WHO guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report. Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 9.
   Short name: WHO TRS 1010, Annex 9
   https://www.who.int/publications/m/item/trs1010-annex9

4. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3.
   Short name: WHO TRS No. 1033, Annex 3
   https://www.who.int/publications/m/item/annex-3-trs-1033

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
   https://www.who.int/publications/m/item/annex-4-trs-929

6. WHO good practices for pharmaceutical quality control laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-seventh Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052), Annex 4.
   Short name: WHO TRS No. 1052, Annex 4
   https://www.who.int/publications/i/item/9789240091030

7. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3.
   Short name: WHO TRS No. 957, Annex 3
   https://www.who.int/publications/m/item/trs957-annex3

8. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8.
   Short name: WHO TRS No. 1010, Annex 8
   https://www.who.int/publications/m/item/Annex-8-trs-1010

9. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-third Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1019), Annex 2.
   Short name: WHO TRS No. 1019, Annex 2
   https://www.who.int/publications/m/item/trs1019-annex2

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
Short name: WHO TRS No. 1044, Annex 4
https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/production/trs1044-annex4-technology-transfer-in-pharmaceutical-manufacturing.pdf

11. WHO good manufacturing practices for sterile pharmaceutical products. Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
Short name: WHO TRS No. 1044, Annex 2
https://www.who.int/publications/m/item/trs1044-annex2

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***
https://www.who.int/publications/m/item/trs943-annex3

13. 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
https://www.who.int/publications/m/item/trs961-annex2

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
https://www.who.int/publications/m/item/trs981-annex2

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
https://www.who.int/publications/m/item/annex-3-trs-981

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.
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https://www.who.int/publications/m/item/tr961-annex14

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