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Prequalification Unit Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Finished Product Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**PharmEvo (Pvt.) Ltd.**
Corporate address of the manufacturer	402, Business Avenue, Block-6, P.E.C.H.S. Shahrah-e-Faisal, Karachi-75400 Pakistan
Inspected site	
Name & address of inspected manufacturing site if different from that given above	PharmEvo (Pvt) Ltd., A-29, North Western Industrial Zone, Port Qasim, Karachi, 75020, Pakistan
Unit/block / workshop number	Tablet section Liquid manufacturing area
Inspection details	
Dates of inspection	12-16 September 2022
Type of inspection	Routine GMP inspection
Introduction	
Brief description of the manufacturing activities	Manufacturing of FPP: a) non-cephalosporin product - OSD (Tablet/ capsule/powder), oral liquid DPI (Dry Powder Inhaler) dosage forms. b) cephalosporin product - OSD (tablet/capsule/suspension powder) and sterile (powder) dosage forms c) Manufacturing of nutraceutical products
General information about the company and site	PharmEvo (Pvt.) Limited was incorporated on the 7th of October 1999, it is a healthcare company, which is engaged in the manufacture, and marketing of pharmaceutical products, including over-the-counter (OTC) medicines, and nutraceuticals. Products manufactured are for the domestic market local consumption as well as for the export markets.
History	This is the third WHO PQ inspection of PharmEvo (Pvt.) Limited, Karachi. The manufacturing site was previously inspected by WHO PQ in July 2018 and March 2020.

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	The following areas were inspected: - Pharmaceutical quality system - Personnel and training - Documentation - Hygiene and sanitization - Process and computerized system validation - Equipment - Production and packaging - Quality control laboratory - Validation and qualification
Restrictions	None
Out of scope	Products and facilities not related to WHO Prequalification
WHO products covered by the inspection	DI009 Zinc (sulfate) Tablet, Dispersible 20mg DI010 Zinc (sulfate) Syrup 10mg/5ml
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
APS	Aseptic process simulation
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GMP	Good manufacturing practices
GPT	Growth promotion test
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high-performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IPA	Isopropyl alcohol
IQ	Installation qualification
LAF	Laminar air flow

LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MFT	Media fill Test
MR	Management review
NC	Nonconformity
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
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
RO	Reverse osmosis
SIP	Sterilization in place
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer
WFI	Water for injection

Part 2	Summary of the findings and comments

1. Pharmaceutical quality system

Generally, a system of Quality Assurance (QA), Good Manufacturing Practice (GMP), Quality Control (QC) and Quality Risk Management (QRM) was implemented. The production and control operations were specified in a written form and GMP requirements were adopted. The managerial responsibilities were specified in the job descriptions.

The product quality reviews were conducted on a calendar basis and all products were divided into 12 months. Minitab software was used to calculate process capability. A template for the PQR report was referenced to the PQR procedure which included a review of starting materials, product contact primary packaging materials, critical in-process controls and finished product results, OOS/OOT, deviations, non-conformances, rework/reprocess and CAPA, changes related to process and analytical methods, variation, stability monitoring and adverse trends, returns, recalls, post-marketing commitment, qualification status, technical agreement and internal audits.

The quality risk management procedure provided two approaches (proactive and reactive) to carry out a risk assessment. The FMEA tool was used to calculate the risk priority number (RPN) using severity (1-5), occurrence (1-5) and detection (1-3).

In addition, other PQS elements such as change controls, deviation management and management reviews were implemented as per the GMP requirements.

The issues raised following the on-site GMP inspection in March 2020 and September 2022 were adequately addressed.

2. Good manufacturing practices for pharmaceutical products

Manufacturing processes were generally defined. Qualifications and validations were adequately performed. Necessary resources were provided, and records were made during manufacture. Procedures were in-place for tracking corrective and preventive actions and their implementation. A system was available to recall any batch of product from sale or supply and complaints about marketed products were examined, the causes of quality defects were required to be investigated, and appropriate measures were taken in respect of the defective products.

PharmEvo is a multi-product non-dedicated manufacturing facility producing medicinal products for different therapeutic areas. The provisions were available to minimize the risks of contamination and cross-contamination using airlocks, buffer rooms, and differential pressures across various processing areas. Zinc sulphate tablets and syrup were produced in a shared facility. It was noted that some of the batches of Zinc Sulfate DS Syrup 20mg/5ml were produced for the export market (Myanmar).

The issues raised following the on-site GMP inspection in March 2020 and September 2022 were adequately addressed.

3. Sanitation and hygiene

The manufacturer had a procedure as the basic approach to personnel hygiene. The changing room was equipped with handwashing facilities. The warehouse and quality control laboratory were found with a satisfactory level of cleanliness.

4. Qualification and validation

A system of qualification and validation of the facility and equipment was in place. Validation Master Plan (VMP) specifies the requirement for all validation-related activities. The VMP applies to process validation, computer system validation, cleaning validation, equipment qualification, facilities & utility qualification, thermal qualification, purified water system qualification, HVAC qualification, transport validation and hold time studies.

Process validation procedure stated that the lifecycle approach should be used for validation processes i.e., stage 1 (process design), stage 2 (process qualification) and stage 3 (continued process verification-CPV). The company manufactured three exhibit batches of Zinc dispersible tablets and Zinc syrup for WHO PQ submission in 2015. The company is required to validate their manufacturing process for both Zinc dispersible tablets and syrup before the commercialization of these products.

The issues raised following the on-site GMP inspection in March 2020 and September 2022 were adequately addressed.

5. Complaints

The procedure for product technical complaints was available. The procedure applied to product technical complaints related to the quality of all pharmaceutical, and nutraceutical products as well as outsourced manufacturers. The Head Quality or designee was responsible for the review, and approval of the investigation and CAPA and periodic review of complaints. Complaints were categorized into three i.e., Class I (Critical), Class II (Major) and Class III (Minor). A complaints logbook was in place.

The issues raised following the on-site GMP inspection in March 2020 and September 2022 were adequately addressed.

6. Product recalls

The procedure for the Management of a product recall was available. The procedure was applied to all products manufactured/imported for marketing by PharmEvo. The different classes and levels of recall were described, i.e., Type A – Consumer/User level, Type B – Retailer level, Type C – Wholesale/distributor level. Mock recalls were performed once every year if no actual recall had taken place.

7. Contract production, analysis and other activities

The manufacture of the PQ products was not subcontracted. In reference to S.R.O 1347(I)2021, DRAP is permitting the contract manufacturing and testing of medicinal products.

8. Self-inspection, quality audits and suppliers' audits and approval

The procedure for self-inspection was available. The head of Quality Operations was responsible for approving self-inspection reports and proposed CAPA. All departments were audited at least once a year and in exceptional cases such as product recall. Self-inspection reports were forwarded to the Head of the department or designee within 15 days. The self-inspection checklists for the different departments were in place. The self-inspection report for the production (Non-Cephalosporin Block) was reviewed.

The issues raised following the on-site GMP inspection in March 2020 and September 2022 were adequately addressed.

9. Personnel

The manufacturer has established an organisational structure, with organograms for overall and specific departments prepared. Key personnel had sufficient qualifications and experiences according to the positions held. The Factory Organogram and Quality Assurance Organogram were discussed. There were two categories of personnel working with the manufacturer, 'staff' and 'contracted staff/worker'.

Contracted staff/ workers were hired based on the applicable procedure. Criteria for contractual staff/worker was defined in the SOP. The Administration department was responsible to handle and coordinate the hiring of contractual staff/workers with the concerned department. Selected candidates were required to undergo the medical test as per the requirement.

Since the last WHO PQ inspection held in March 2020, the company had recruited the General Manager of Quality Operations who is overseeing the overall activities of quality control and quality assurance.

The issues raised following the on-site GMP inspection in March 2020 and September 2022 were adequately addressed.

10. Training

The SOP for the employee's training program described how training needs were identified and annual training plan was prepared. Different types of training were conducted as orientation programs, visitor training, on-job training, GMP refresher, and external training for contract staff and management staff. The training was imparted through the classroom, read-only and verbal training. At the end of the training, it was assessed using a questionnaire with passing marks above 70%. Retraining was imparted if the trainee scored less than 70% marks. The HR head was responsible for maintaining an updated list of management staff, while Admin & Security head was responsible for maintaining an updated list of non-management staff.

Training records on SOP for entry and exit in the Cephalosporin area, refresher GMP training, personal hygiene and entry and exit in the sterile area were reviewed.

The issues raised following the on-site GMP inspection in March 2020 and September 2022 were adequately addressed.

11. Personal hygiene

The gowning procedure was defined in the SOP. The manufacturer used a blue-coloured gown for personnel working in Pharmaceutical Plant (the non-cephalosporin manufacturing facility) and a green-coloured gown for personnel working in Nutraceutical Plant. There was an additional dark blue stripe at the collar and sleeve of blue coloured gown provided for personnel working in the Cephalosporin Plant. 70% IPA was used as a hand sanitiser and provided at the entrance of the facility. QA staff, production staff and production workers were dedicated to the Cephalosporin area. It was noted that a dedicated laundry facility was part of the Cephalosporin block area whereas, for non-Cephalosporin block, services were outsourced.

The gowning procedure was found adequate as 2 pieces suit along with a hairnet, face mask and shoe cover were required before entering to the manufacturing facility. Separate change rooms were provided for visitors and staff. 70% IPA was used as a disinfectant.

The issues raised following the on-site GMP inspection in March 2020 and September 2022 were adequately addressed.

12. Premises

The pharma plant consists of:

- Basement - Warehouse of raw material & primary packaging material and sampling facility
- Ground floor - Production facility, packaging material warehouse and finished product warehouse
- Mezzanine floor - Product development laboratory, Quality Control laboratory, offices, and technical area for utilities
- First floor - canteen

The plan layout was documented in the document, ‘Proposed Building of PharmEvo (Pvt) Ltd at Port Qasim, Karachi; revised basement and a document titled ‘Submission Plan Ground Floor Pharmaceutical. Generally, the premises and equipment were located and maintained to suit the operations carried out.

The issues raised following the on-site GMP inspection in March 2020 and September 2022 were adequately addressed.

13. Equipment

Equipment used by the manufacturer was located and maintained to suit the operations to be carried out. Manufacturing equipment for mixing/blending, compression, and blistering process were available in each respective room. Testing equipment was available in the laboratory. Balances and other measuring equipment were found calibrated according to a fixed schedule.

All blister rooms were equipped with a blister machine. One calibrated thermohygrometer was available in each blister room for temperature and relative humidity monitoring. All compression rooms were equipped with a compression machine. QC instrument lab was equipped with 11 HPLCs. GC and AA instruments were kept specifically in the GC and AA Room. The usage and records of one HPLC were reviewed and discussed. The packaging material sampled was tested/verified by the packaging material laboratory. The sampling and testing performed were discussed. One unit of calibrated Vernier calliper was available in the Packaging Material Laboratory. The calibration documents for the Vernier calliper were reviewed.

The issues raised following the on-site GMP inspection in March 2020 and September 2022 were adequately addressed.

14. Materials

There was a procedure in place for receiving incoming materials which were eventually quarantined, sampled and approved before being used. Incoming materials were received at the receiving area located on the ground floor. The weight of the material received was verified using one calibrated weighing balance. The balance was verified using calibrated standard weight daily and recorded in the verification record. The pest control program (bait station for rodents' control) was available in this area. The raw material and primary packaging materials were received and kept in the raw material store located in the basement. The temperature and humidity were controlled as per specification, 23±2°C and 65%. The storage temperature was monitored using calibrated data logger at the identified location. The data from the logger were downloaded and printed weekly by the warehouse personnel. The empty hard gelatin capsules were stored at temperature and humidity-controlled room. The humidity was controlled using a portable dehumidifier unit located in the room. There were separated quarantine area and approve area and was locked appropriately. Sampling room facilities for raw materials were located in the basement, connected with the quarantine area. Racking system with specified location identification. was available. Raw material and primary packaging material were given a 'Quarantine' label and a 'Sampled' label following the sampling in the sampling room. The approved label was affixed once the material was approved by the quality department.

The approved raw material was dispensed by the warehouse personnel in the dispensing room. The dispensed materials with BMR documents were kept at the staging dispensed area in a locked cage. The material was then taken to the respective processing room for the manufacturing process. There were storage rooms to keep the intermediate product. An inventory of intermediates was recorded. The finished products were stored in the Finished Good warehouse until the product was approved for distribution.

The issues raised following the on-site GMP inspection in March 2020 and September 2022 were adequately addressed.

15. Documentation

The manufacturer had established a documentation system where it constituted an essential part of the Quality Assurance System. The SOPs were prepared, reviewed, approved, signed and dated by the appropriate personnel. A paper-based system exists for the management of documents such as SOPs, and methods.

The issues raised following the on-site GMP inspection in March 2020 and September 2022 were adequately addressed.

16. Good practices in production

Access to production was restricted and controlled by the biometric system. Change room and locker room were provided for the production personnel. The personnel's shoes were removed and kept in the locker room. The street clothes were removed in the 1st Change room and the production uniform was used in the 2nd Change Room. Lockers were provided in all the rooms. There were rooms prepared for cleaning activities and storing cleaning utensils. The Wash area was used to clean the manufacturing equipment/equipment parts or containers. Cleaning utensils such as mops and wipes used by the cleaner in the manufacturing area were kept in the Janitor's Room.

The manufacturing area was classified as Grade D (Class 100,000). The core processing areas were equipped with separate MAL and PAL (liquid section) whereas the tablet section had buffer rooms before entering the core processing areas. At the time of the inspection, differential pressure, temperature, and relative humidity were monitored and recorded manually. A Building Management System (BMS) was under installation at the time of the Inspection.

There were some manufacturing activities carried out during the inspection in the tablet manufacturing area. However, no manufacturing activity was carried out in the liquid manufacturing area during the inspection. The company informed the inspectors that there are only two liquid products which are not regularly manufactured.

The issues raised following the on-site GMP inspection in March 2020 and September 2022 were adequately addressed.

17. Good practices in quality control

The quality control laboratory was located separately and independent of the production activities. The QC manager reports to the General Manager of Quality Operations who in turn reports to the company's Chief Operating Officer.

The laboratory was equipped with HPLC, GC, AAS, Melvern Mastersizer, UV, IR and other sophisticated equipment and instruments. Since the last WHO PQ inspection, the company had implemented a networked-based system for all the chromatographic data systems. The procedure for access management was developed and implemented.

The laboratory was equipped with several stability chambers which had an alarm system.

The laboratory also had a retention sample room for reserving samples from raw materials and finished products.

The issues raised following the on-site GMP inspection in March 2020 and September 2022 were adequately addressed.

Part 3	**Conclusion – Inspection outcome**

Based on the areas inspected, the people met and the documents reviewed and considering the findings of the inspection, including the observations listed in the Inspection Report, ***PharmEvo (Pvt.) Ltd,*** located at ***A-29, North Western Industrial Zone, Port Qasim, Karachi, Pakistan*** was considered to be operating at an acceptable level of compliance with WHO GMP 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://digicollections.net/medicinedocs/documents/s21467en/s21467en.pdf

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***
   untitled (digicollections.net)

3. 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
   9789240020900-eng.pdf (who.int)

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
   https://digicollections.net/medicinedocs/documents/s21440en/s21440en.pdf

5. 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://digicollections.net/medicinedocs/documents/s23455en/s23455en.pdf

6. 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
   https://digicollections.net/medicinedocs/documents/s20108en/s20108en.pdf

7. WHO good practices for pharmaceutical quality control laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1.
   Short name: WHO TRS No. 961, 957), Annex 1
   https://digicollections.net/medicinedocs/documents/s18681en/s18681en.pdf

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
https://digicollections.net/medicinedocs/documents/s22358en/s22358en.pdf

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
https://digicollections.net/medicinedocs/documents/s19959en/s19959en.pdf

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
https://digicollections.net/medicinedocs/documents/s18677en/s18677en.pdf

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***
https://digicollections.net/medicinedocs/documents/s18683en/s18683en.pdf

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://digicollections.net/medicinedocs/#d/s21438en

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://digicollections.net/medicinedocs/documents/s18682en/s18682en.pdf

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://digicollections.net/medicinedocs/#d/s20177en/

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://digicollections.net/medicinedocs/#d/s20175en/

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. Good Manufacturing Practices: Guidelines on validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3. ***Short name: WHO TRS No. 1019, Annex 3***
https://digicollections.net/medicinedocs/documents/s23697en/s23697en.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***
Essential Medicines and Health Products Information Portal (digicollections.net)

20. WHO Recommendations for quality requirements when plant – derived artemisin is used as a starting material in the production of antimalarial active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 6
Short name: WHO TRS No. 992, Annex 6
https://www.who.int/publications/m/item/who-recommendations-for-quality-requirements-when-plant-derived-artemisinin-is-used-as-a-starting-material-in-the-production-of-antimalarial-active-pharmaceutical-ingredients---trs-992---annex-6

21. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4. ***Short name: WHO TRS No. 1033, Annex 4***
9789240020900-eng.pdf (who.int)

22. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
Short name: WHO TRS No. 996, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

23. Stability testing of active pharmaceutical ingredients and finished 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 10.
Short name: WHO TRS No. 1010, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

24. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditionning 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://digicollections.net/medicinedocs/documents/s23699en/s23699en.pdf

25. Points to consider when including Health-Based Exposure Limits in cleaning validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 2. **Short name: WHO TRS No. 1033, Annex 2**
9789240020900-eng.pdf (who.int)

26. Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 6. **Short name: WHO TRS No. 1025, Annex 6**
9789240001824-eng.pdf (who.int)

27. Production of water for injection by means other than distillation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 3. ***Short name: WHO TRS No. 1025, Annex 3***
https://www.who.int/publications-detail/978-92-4-000182-4

28. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4. ***Short name: WHO TRS No. 1025, Annex 4***
https://www.who.int/publications-detail/978-92-4-000182-4