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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	**Remington Pharmaceutical Industries (Pvt) Ltd**
Corporate address of manufacturer	18 km Multan Road, Lahore 53800, Pakistan
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Remington Pharmaceutical Industries (Pvt) Ltd 18 km Multan Road, Lahore 53800, Pakistan D-U-N-S Number: 645601865 Global Positioning System Details (GPS): Latitude: 31.438678 N *Longitude: 74.192108*
Unit / block / workshop number	Oral solid dosage form section (tablet manufacturing)
Inspection details	
Dates of inspection	19-23 April 2021
Type of inspection	Follow-up GMP inspection
Introduction	
Brief description of the manufacturing activities	Remington produces sterile and non-sterile pharmaceutical products according to the Manufacturing License No. 000061 issued by the Central Licensing Board, Government of Pakistan. The company produces tablets, dry suspension, oral liquid, ointment, cream, lotion, sterile eye drops, eye ointment and ear/nose and throat preparations. In addition, Remington carries out packaging activities and quality control testing (physical, chemical and microbiological). No activities other than pharmaceutical manufacturing are performed.
General information about the company and site	Remington was established almost 45 years ago, and it is located at 18 Km Multan Road, Lahore in Pakistan. As per the site master file, finished products of Remington are distributed not only within Pakistan but also to various other countries based on applicable distribution agreement i.e Afghanistan, Sri Lanka, Vietnam, Philippines, Kenya, Myanmar, Sudan, Cambodia, Maldives, Uzbekistan, Kyrgyzstan, Tajikistan and Uganda.
History	WHO PQ inspection team has inspected Remington previously with this being the fourth fifth PQ inspection. The last inspected by the PQ team was performed in March 2020

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	A follow-up inspection was limited to verification of corrective actions and preventive actions for the deficiencies raised during the March 2020 PQ inspection. The following areas were inspected: a) Pharmaceutical quality system (PQS) b) Calibration and qualification c) Equipment d) Premises e) Documentation f) Quality control laboratory
Restrictions	Due to the ongoing Covid-19 situation and fasting month, the inspection was performed between 9 am and 4 pm from Monday to Friday.
Out of scope	The scope of this inspection was limited to the oral solid dosage form section, in particular, manufacturing of Levofloxacin tablets 250mg.
WHO products covered by the inspection	Levofloxacin Tablet, Film-coated 250mg (TB381)
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
CEF	Cleaning Effectiveness Factor
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
HBEL	Health-based exposure limit
HPLC	High performance liquid chromatography (or high-performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning

IQ	Installation qualification
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MFT	Media fill Test
MSC	Maximum Safe Carryover
MSSR	Maximum Safe Surface Residue
MR	Management review
NC	Non conformity
NRA	National regulatory agency
OQ	Operational qualification
PDE	Permissible Daily Exposure
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

In general, there was an adequate pharmaceutical quality system (PQS) implemented by Remington in accordance with WHO GMP Guidelines. The company had implemented several systems and procedures based on the feedback given during the last PQ inspection in March 2020. In general, production and control operations were independently managed and GMP requirements were generally followed. The following PQS elements were inspected:

Product quality review (PQR) of Levofloxacin (as hemihydrate) 250mg tablet for the period of Jan-Dec 2020 was discussed. The company has so far manufactured three batches for PQ submission. Based on the comments received from the previous WHO PQ inspection held in March 2020, the company has revised the PQR procedure and updated the PQR of Levofloxacin tablets in detail and provided better clarity. The company has not produced any batch of Levofloxacin tablet in 2020 and 2021 (to-date). It should be noted that the company produces Levofloxacin tablet for the domestic market using different formulation (source of API, formulation, dimension etc). A separate change control was raised to convert the domestic formulation into the WHO PQ submitted formulation. One batch has been manufactured, with the same formulation as was developed for WHO PQ, in June 2021.

In general, the revised PQR procedure considered adequate.

Incidents and deviations management procedure was updated since the last PQ inspection. The revised procedure covered both incidents and deviations which are now recorded under event form. The procedure applied to incidents about warehouse, manufacturing, packing, QC, QA, RND, engineering, IT and other areas. The procedure stated that planned deviations are handled through a change control procedure. The term "event" was described as an unexpected occurrence and categorized into incident and deviation. The procedure stated that OOS/OOT, environmental monitoring, in-process control tests and stability failures are handled through separate procedures. The procedure was supported with a deviation form. The initial impact assessment was performed by the respective department before QA categorized deviation into critical, major and other. A formal root cause analysis (RCA) is performed if a deviation is classified as major or critical. A separate procedure was followed for RCA. In general, the revised procedure considered adequate.

Change controls procedure was discussed. The revised procedure was supported with a detailed change control form including but not limited to initial impact assessment, classification of change, type of change and risk assessment (only limited to Level 3 changes). Change control logbook for 2020 and 2021 was maintained covering the information such as change control number, change control raised by/date, change control raised by department/area, description of the change, the criticality of change (minor/major), implementation date and extended implementation date. The following change controls were reviewed:

- Change control about up-gradation of OSD area was discussed. The change was categorized as major (permanent) and a formal risk assessment was performed. The change was supported with existing & proposed layouts, URS, area qualification protocol, risk assessment etc. The change was closed on 14/12/2020.
- Change control about the installation of autosampler to HPLC was discussed.

Change control trending report (July-Sept 2020) was discussed. During this period, a total of 70 changes were initiated (27 Major and 43 Minor). Most of the changes were initiated by the RND department. It was concluded that the change control system is adequately implemented. Change control trending report (Jan-Mar 2021) was discussed.

In general, the inspection team had observed improvement in the handling of change control management. It was commented that a holistic approach be adopted for all change controls ensuing justification for classification, risk assessment and availability of supporting documents.

Quality risk management (QRM) report was reviewed. The risk assessment was performed to assess the risk associated with the up-gradation of the OSD facility in the OSD production department. The QRM report was supported with a process flow chart starting from raising change control, quality risk management, approval of change control, URS approval, purchase order, installation, qualification of airlocks, preparation of relevant SOPs, performance qualification and routine operation. In general, this is considered adequate.

Health-based exposure limit (HBEL): As Remington has a multiproduct or shared manufacturing facility for different therapeutic products, the company has introduced a system of HBEL to assess risks in cleaning validation based on the deficiency raised during the last PQ inspection in March 2020. Considering various products (tablets, capsules, dry suspension, oral liquid, external preparations, sterile eye drops) produced by Remington, a cleanability protocol was drafted. The cleanability test for Levofloxacin 250mg tablet was reviewed. The test was performed in the R&D lab. The cleaning effectiveness factor (CEF) was calculated based on "cleaning process development: cleanability testing and hardest to clean pharmaceutical products" (ASTM G121 and G122 standards). A separate document title "Maximum safe carryover (MSC) and Maximum Safe Surface Residue (MSSR) calculation" was discussed. The purpose of this document was to calculate the MSC and MSSR limit for all the tablets manufactured in the OSD section. Based on the MSCand MSSR studies, the company had concluded that Ketotifen 1mg tablet has the highest cleaning effectiveness factor and therefore cleaning validation was required to be performed. The cleaning validation was performed and completed.

The revised cleaning validation procedure was discussed. The pre-requisite, to carry out cleaning validation, was described in the procedure. It stated that permissible daily exposure (PDE) reports of active pharmaceutical ingredients and coupons for the cleanability test must be available before pursuing cleaning validation. The procedure also made provision for campaign hold time cleaning validation, uncleaned equipment hold time study, clean equipment hold time study and revalidation frequency. The cleaning validation will be repeated if there is a change in any of the critical parameter i.e. cleaning procedure, change in batch size (more than 10%), use of detergents or change in formulation. Periodic revalidation will be carried out after three years. In general, the company had implemented an adequate

PDE approach to ensure carryover from the previous product is removed or remained below the PDE limit to the next product.

The deficiencies noted from the pharmaceutical quality system section have been addressed satisfactorily and the same will be verified during future PQ inspections.

2. Good manufacturing practices for pharmaceutical products

Since the last PQ inspection of March 2020, the company has upgraded the OSD section area. The up-gradation has provided better controls in terms of movement of personnel and materials which in turn will ensure contamination and cross-contamination requirement. A visit to the OSD section was made to verify the implementation of action plans.

The deficiencies noted from the GMP for pharmaceutical products section have been addressed satisfactorily and the same will be verified during future PQ inspections.

3. Sanitation and hygiene

From a brief visit to the OSD section facility, it was noted that the changing rooms were equipped with handwashing and gowning facilities. The manufacturing area, packaging area, warehouses and quality control laboratory were found with a satisfactory level of cleanliness at the time of inspection The deficiencies noted from the pharmaceutical quality system section have been addressed satisfactorily and the same will be verified during future PQ inspections.

4. Qualification and validation

The up-graded area of the OSD section was briefly inspected and found to be adequate. In addition, the following qualification documents were reviewed:

- HVAC system performance qualification report of OSD section summarized that tests such as HEPA filter integrity, airflow visualization, air volume, room air changes per hour and recovery test were performed by third parties and found to be satisfactory. Tests such as non-viable count, viable count, pressure differentials, temperature and relative humidity were performed by in-house engineers and reported to be within the acceptance limit. HEPA filter integrity test was performed in January 2020 by the contract party. The test is performed once per year. In general, it is considered satisfactory.
- *Qualification of a camera system for blister packing machine:*
  URS for camera system of blister packing machine was discussed. The camera was installed after the feeder and before the sealing section to detect the missing tablet or broken tablet in each blister during operation. The URS described technical requirements such as detection of the missing tablet, minimum 5-15% broken tablet, minimum 5-15% chipped, colour mismatch and other product tablets. Design qualification protocol of the camera inspection system on the blister machine was discussed. The URS compliance check was performed as part of DQ. Operational qualification protocol of the camera inspection system on the blister machine was discussed. Performance qualification protocol of blister machine was discussed. The company has performed requalification of the entire blister packing machine including the camera system using placebo tablets. The camera rejection sensor challenge test was performed to confirm empty

blisters, broken or chipped tablet and different colour tablet. The SOP for blister packing machine operation and cleaning was revised and made effective after incorporating instructions for the usage of the camera system.

The deficiencies noted from the qualification and validation section have been addressed satisfactorily and the same will be verified during future PQ inspections.

5. Complaints

Handling of customer complaints was briefly discussed. The procedure was revised in August 2020 following the comments made by the WHO PQ inspection team in March 2020. The following documents related to the handling of complaints were reviewed:

- Customer complaint logbook for 2021 was discussed. A complaint was received in 2021 for a short pack. The company has identified that the selection criteria for the weight limit of the outer carton in BPR were not properly defined. The company has now revised their acceptance criteria for carton weight across all products.
- Quarterly customer complaint trending report for the first quarter of 2021 was available. Similarly, a complaint trending report for all quarters of 2020 was in place. In addition to performing a quarterly review, the company is recommended to perform annual trend analysis. The complaints are tracked through a validated spreadsheet as indicated by the company.

In general, the complaint handling procedure provided greater clarity. The company is recommended to ensure that each complaint is holistically and collectively investigated, and corrective and preventive actions are sustainable.

The deficiencies noted from the complaint section have been addressed satisfactorily and the same will be verified during future PQ inspections.

6. Product recalls

Product recall procedure was discussed. No product recalled was initiated in 2020 and 2021. Two mock recalls were initiated in 2020 covering the domestic and export market. In general, the product recall procedure is considered adequate. The company is required to adhere to their SOP.

The deficiencies noted from the product recalls section have been addressed satisfactorily and the same will be verified during future PQ inspections.

7. Contract production, analysis and other activities

The company reconfirmed that manufacturing and laboratory activities related to Levofloxacin 250mg film-coated tablets are not outsourced. The company used several vendors for carrying out calibration, qualification and requalification of equipment and instruments. A written contract between the company and the contractor for calibration service of UV, HPLC, GC, TOC & FTIR with quality agreement was discussed. The responsibilities of each party, covering the outsourced activities, was established in the contract.

The company was required to review and assess the records and results related to the outsourced activities and ensure that all products and materials used in the calibration activities by the vendor were adequately certified and the documentation complied with the applicable procedures.

The deficiencies noted from the contract production, analysis and other activities have been addressed satisfactorily and the same will be verified during future PQ inspections.

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

The self-inspection program was designed to detect the shortcomings in the implementation of GMP activities and to recommend the necessary corrective actions in accordance with the SOP. The Self-inspections plans for June and October 2020 were discussed. The team responsible for self-inspection consisted of personnel who could objectively evaluate the activities. A list of personnel attending each inspection was provided in advance to the inspection plan. During the audit, all activities were covered with a focus on findings from the preceding inspection, followed by a selection of new areas to be audited based on the auditors' assessment.

The recommendations for corrective action were implemented in CAPA Tracker format (for each respective department), where the information about observation, root cause analysis, correction and proposed corrective action, effectiveness, target timeline, assessment by auditor and status with the closing date was mentioned. In addition, an Excel sheet to track all the CAPAs was available and monitored by the responsible department until the respective observation was closed.

The deficiencies noted from the self-inspection, quality audits and suppliers' audits and approval have been addressed satisfactorily and the same will be verified during future PQ inspections.

9. Personnel

The manufacturer had an adequate number of personnel with the necessary qualifications and practical experience.

The deficiencies noted from the personnel section have been addressed satisfactorily and the same will be verified during future PQ inspections.

10. Training

The personnel were trained following SOP on the training of personnel. A document titled "Training Need Analysis (TNA)" was annually prepared for each department with information about the name of SOPs, as well as roles and personnel required to receive the respective training. Randomly selected TNA, training plan, training documentation and the respective attendance list were reviewed.

The deficiencies noted from training section have been addressed satisfactorily and the same will be verified during future PQ inspections.

11. Personal hygiene

Gowning procedure to enter the warehouse and productions facilities was in place. Hand washing facility, mirror and production gown procedure were provided in the change rooms. Separate change rooms (for staff and visitors) were in place. In general, the gowning procedure was found adequate and was supported with SOPs and pictorial presentation.

The deficiencies noted from the personal hygiene section have been addressed satisfactorily and the same will be verified during future PQ inspections.

12. Premises

Since it was a follow-up inspection, the inspection team did not visit the entire manufacturing facility.

From the PQ inspection held in March 2020, there were three buildings; factory building, utilities & workshop building and administration block. On the ground floor of factory building, there was the OSD manufacturing and packaging area, dispensing area equipped with 3 RLAFs, staging areas and warehouse. On the first floor, there was the analytical and microbiology laboratory, the RND laboratory, stability room, PW system (with separate entrance) and on the second floor, there was the printing area for labels and cartons and the packaging materials staging area.

Generally, premises were located, designed, constructed, adapted, and maintained to suit the operations being carried out. Only authorized persons could enter the production areas and warehouses. This was controlled through biometric devices. The same entry was used for personnel and visitors to production facilities, but different rules applied to gowning rooms for visitors and staff. The production area was laid out to allow production to take place in areas connected in a logical order corresponding to the sequence of the operations and the requisite cleanliness levels. Exposed surfaces were smooth, impervious and unbroken to minimize the shedding or accumulation of particles or microorganisms and permitted the application of cleaning agents.

Storage areas were of sufficient capacity. Receiving and dispatch bays were separated and protected materials and products from the weather. There was a staging area, quarantine area for raw materials, raw materials approved area, packaging materials quarantine and packaging materials approved.

QC laboratory was separated from production areas and was well equipped.

Process areas were classified as Grade D. Supply air was filtered through filters G4, bag filters F6 and F9 and terminal HEPA filters H13. Recirculated air was a mixture of 15% fresh and 85% return air. The logbook of cleaning bag filters and the logbook of recording the Δp of filters were reviewed. Positive pressure was maintained in the main production corridor concerning processing rooms. Temperature and relative humidity were maintained within defined limits.

The deficiencies noted from the premises section have been addressed satisfactorily and the same will be verified during future PQ inspections.

13. Equipment

In general, the production and laboratory equipment were located, designed, constructed, adapted and maintained to suit the operations to be carried out. The layout and design of equipment were appropriate to minimize the risk of errors and permit effective cleaning and maintenance to avoid cross-contamination, build-up of dust or dirt. An ongoing programme based on a regular review of equipment qualification was implemented. The site was committed to continuously maintain the validation status which was stated in the site's validation master plan. The responsibility and procedures for performing validation were defined in the respective SOPs. Calibration and qualification activities were conducted by following predefined and approved protocols and a written report summarizing the results and the conclusions were prepared. The reports were available upon request.

The deficiencies noted from equipment section have been addressed satisfactorily and the same will be verified during future PQ inspections.

14. Materials

From the PQ inspection held in March 2020, incoming materials and finished products were quarantined after receipt until they were tested and released for use in production.

Vendor/supplier qualification procedure was discussed which provided stepwise instruction for vendor approval of APIs, excipients, primary & secondary packaging materials, laboratory chemicals and solvents. The qualification was performed by on-site audit or by questionnaire. An approved supplier list (imported raw materials) was in place which identified two sources of Levofloxacin Hemihydrate. From the review of the supplier qualification report, it was noted that the initial desktop assessment was performed in August 2018 which was again reassessed in December 2019 using a questionnaire.

Rejected materials and products were marked as such and stored separately.

The deficiencies noted from the materials section have been addressed satisfactorily and the same will be verified during future PQ inspections.

15. Documentation

Generally, the manufacturer had established an essential documentation system as part of the Quality Assurance System. Several documents and raw data were reviewed. Documents were approved, signed and dated by the appropriate responsible persons. None of the reviewed documentation was not found to have been changed without prior authorization and approval.

Documents had unambiguous contents: the title, nature and purpose were clearly stated. Reproduced documents were clear and legible. The reproduction of working documents from master documents was considered to be controlled documentation by having a general reference document number. The entries were clear, legible and indelible. Enough space was provided for such entries. Any alteration made to a document was signed and dated, and the alterations were made in such a way as to permit the reading of the original information. Where appropriate, the reason for the alteration was recorded. Records were made or completed when any action was taken. Records were retained for at least one year after the expiry date of the finished product following their procedures.

By reviewing the LabSolution software system, it was noted that only authorized persons had rights to enter or modify data in the computer system, and there was an adequate audit trail to record changes and deletions. Access was restricted by passwords and the entry of critical data was independently checked by QA-reviewer. Records were stored electronically and protected by backup transfer to a server following the applicable SOP on an ongoing basis at the time of data generation. The data were readily available. Randomly selected projects were restored once a year by verifying the technical and factual content of folders.

The deficiencies noted from the documentation section have been addressed satisfactorily and the same will be verified during future PQ inspections.

16. Good practices in production

The production and packaging areas was briefly visited. In general, production and packaging areas were found to be clean, tidy, well-lit and properly maintained. At the time of the inspection, no production activities were being carried out.

All manufacturing areas for Levofloxacin 250mg film-coated tablet were visited in March 2020. Levofloxacin 250mg film-coated tablets were produced in a shared OSD facility. Areas inspected included storage rooms, dispensing area, granulation, blending, compression rooms, coating room, IPC, washing room, tool rooms, primary and secondary packaging areas. The secondary packaging was done manually.

The deficiencies noted from the production section have been addressed satisfactorily and the same will be verified during future PQ inspections.

17. Good practices in quality control

Quality Control (QC) operations were separated from the production operations. The QC was composed of an analytical laboratory, microbiology laboratory and RND laboratory/department. The laboratory had a QC function. The QC function was independent of other departments and under the authority of a staff member with appropriate qualifications and experience. Adequate resources were available to ensure that all the QC arrangements were properly carried out.

Facilities, trained personnel and approved procedures were available for laboratory related activities, qualification and validation. Records were made (manually and/or by recording instruments) demonstrating that all the required sampling, inspecting and testing procedures had been appropriately carried out.

Records were made in "Templates for approved reports". Executive reports were prepared using the results of inspecting and testing data against specifications by following the respective protocol and STM. Samples of starting materials and products were retained to permit future examination of the product, if necessary.

Reference and working standards were provided, maintained and stored.

It was ensured that the stability of the active pharmaceutical ingredients and products were monitored as per the applicable plan. The main stability plan was stored in an Excel sheet, which was the basis of a manual monthly plan. The manual monthly plan directed the schedule of the respective stability tests.

The deficiencies noted from the quality control section have been addressed satisfactorily and the same will be verified during future PQ inspections.

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, ***Remington Pharmaceutical Industries (Pvt) Ltd,*** located at ***18 km Multan Road, Lahore 53800, 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***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

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***
http://www.who.int/medicines/publications/44threport/en/

3. 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

4. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4. ***Short name: WHO TRS No. 937, Annex 4***
http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf?ua=1

5. 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

6. 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. 957, Annex 1***
http://www.who.int/medicines/publications/44threport/en/

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***
http://www.who.int/medicines/publications/44threport/en/

8. 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

9. 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

10. 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

11. 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

12. 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

13. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2. ***Short name: WHO TRS No. 981, Annex 2***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

14. WHO 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/

15. 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

16. 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

17. WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5. ***Short name: WHO TRS No. 992, Annex 5***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

18. 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 Multisource guidance*** or ***WHO TRS No. 996, Annex 10***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

19. 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/

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