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Prequalification Team Inspection Services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Active Pharmaceutical Ingredient Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**Macleods Pharmaceuticals Ltd (UNIT- X)**
Corporate address of the manufacturer	Atlanta Arcade Marol Church Road, Andheri East Mumbai, Maharashtra ZIP Code: 400 059 India
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Plot No. D-3/27, GIDC Dahej-III, Village: Sambheti, District: Bharuch, State: Gujarat, PIN: 392130, India Latitude: 21º.76'637" N & Longitude: 72º.66'396" E DUNS number: 854247786
Synthetic unit /Block/ Workshop	Rifampicin, Module III, Block D Levofloxacin, Module II, Block D Rifapentine Stage-I, Block A
Inspection details	
Dates of inspection	21-25 October 2024
Type of inspection	Initial GMP inspection
Introduction	
Brief description of the manufacturing activities	This manufacturing site manufactures KSMs, Intermediates, and APIs. It is located in the GIDC, Dahej industrial area. It is surrounded by open land. The total area of the site is 1,59,580.085 m^2, which is covered by buildings and open gardens; the total built-up area is 28,798.58 m^2. The Unit-X Dahej site was established in 2022. This facility has a multi-product manufacturing Block - A, for KSMs and intermediates, and a manufacturing block -C, for the solvent recovery plant (SRP). Manufacturing Block-D for intermediates and APIs, Manufacturing Block-E, and Block-F are under construction and shall be used for Fermentation & DSP-2, respectively.
General information about the company and site	Macleods Pharmaceuticals Limited is an integrated pharmaceutical company that produces finished dosages and active pharmaceutical ingredients. The company was established in 1986 to manufacture pharmaceutical products. The company has its corporate office in Andheri, Mumbai. It has nine manufacturing units at various locations in India, an R&D center in Mumbai, and approximately 20,000 employees associated with the company in various departments. - Pharmaceuticals Formulation (Unit-I), Palghar (District Thane) - Pharmaceuticals Formulation (Unit-II), Daman (Union Territory) - Pharmaceuticals Formulation (Unit-III), Daman (Union Territory)

	- Research & Development (R&D) Centre, Andheri (Mumbai) - Active Pharmaceutical Ingredient (Unit-V), Sarigam, (Gujarat) - Pharmaceuticals Formulation (Unit-VI), Nalagarh, (Himachal Pradesh) - Pharmaceuticals Formulation (Unit-VII), Daman (Union Territory) - Pharmaceuticals Formulation (Unit-IX), Sikkim - Key starting materials, intermediates, and APIs (Unit-X), Dahej (Gujarat) - Pharmaceuticals Formulation (Unit-XI), Pithampur, Indore (Madhya Pradesh)
History	This was the first WHO PQ inspection of the Macleods Pharmaceuticals Ltd. manufacturing site located at Dahej, Gujarat. The CDSCO and Gujarat FDCA inspected the site in September 2024 and granted the GMP certificate. Additionally, from 29th May to 2nd June 2023, the USFDA conducted an inspection of the Levofloxacin Stage-II production process.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	The following areas were inspected: 1. Quality management 2. Quality control laboratories (physical, chemical, and microbiology) 3. Premises and process equipment 4. Qualification and validation 5. Self-inspection, quality audits, and supplier qualification 6. Production and packaging operations 7. Storage and distribution 8. Purified water system 9. Air handling units 10. Solvent farm tank
Restrictions	None
Out of scope	The products (intermediates and APIs) not submitted for the WHO PQ were outside the scope of this inspection.
WHO APIs covered by the inspection	1. Rifampicin 2. Levofloxacin 3. Stage-I intermediate (3-formyl rifamycin SV), Rifapentine (APIMF375)
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA+	Attributable, legible, contemporaneous, original, and accurate and complete, consistent, enduring, and available.
API	Active pharmaceutical ingredient
APR	Annual product review
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
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
HEPA	High efficiency particulate air
HPLC	High-performance liquid chromatography (or high-performance liquid chromatography equipment)
HVAC	Heating, ventilation, and air conditioning
IQ	Installation qualification
KF	Karl Fisher
KSM	Key Starting Material
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
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
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer

Part 2	Summary of the findings and comments

1. Quality management

The quality management system was established, documented, and implemented, as noted in the review of various documents and records. The following electronic systems were used for quality management:

TrackWise	Change controls, complaints, deviations, OOS, lab incidents, and CAPA
Document Management System	SOPs, specifications, and standard testing procedures
SAP	Material management, quality system (batch release)
Personal Learning Management System	Training purposes
Caliber LIMS	Analytical records
Chromeleon 7.3	Chromatography (HPLC and GC).

The manufacturing site had a separate quality unit independent of production, comprised of quality assurance and quality control, which reports separately to the corporate quality head based in Mumbai, India. The responsibilities of the quality unit were described in the respective job descriptions of quality personnel, which included reviewing quality-related documents and releasing or rejecting all APIs, intermediates, key starting materials, and starting materials. Similarly, the responsibilities of the production department were described in the respective job descriptions and mainly included producing APIs and other materials as per the approved manufacturing instructions.

The quality assurance manual described all the relevant GMP aspects, including quality policy, validation, premises qualification, material management, personnel, complaint-recall, deviation, change control, quality risk management, etc.

The product quality review (PQR) procedure guided the performance of PQR for starting materials and finished products (APIs) manufactured in Unit-X. The procedure described the definitions of PQR, CPPs, CQAs, trends, and control limits. The PQR was performed on a rolling basis, but based on the anniversary of the approval date after filing the dossiers. The procedure stated that PQR would be conducted for all products regardless of the number of batches manufactured. The contents of the PQR were in line with the WHO GMP for APIs and intermediates. Based on the review of the PQR, the PQR report was classified into Levels 1, 2, and 3, and appropriate action was recommended. The analytical data were collected from the LIMS, and an Excel sheet was used for the statistical data interpretation.

The quality risk management (QRM) procedure was reviewed and noted that it applied to the system, product, process, equipment, facility, and quality management system. The procedure described the responsibilities and definitions of various terms used. The procedure provided references to FMEA and HACCP (using OEB); The risk registers related to products and non-product risk assessment were maintained. In 2024, 55 product risks were assessed, including risk assessment pertaining to Rifampicin introduction. Nonproduct-related risk assessment included facility, complaint, recalls, and new equipment introduction; 43 risks were evaluated in 2024.

The data integrity policy was available. The policy was prepared following the references from the UK MHRA, WHO, USFDA, and other authorities. The SOP on the code of conduct on DI and management of GMP violations was reviewed. It provided a procedure for handling data integrity (DI) issues. A protocol for risk assessment study (FMEA analysis) on data integrity (RAP/24036 dated 30/08/2024) was prepared to assess risk associated with the Good Data Management and data generated by electronic and paper-based systems during manufacturing, operation, analysis, training, inspection, documentation, and backup.

The contamination control strategy (CCS) of the API manufacturing facility was initiated to assess the risk associated with the APIs and intermediates manufacturing operation. The main elements of CCS included the design of the plant, premises, equipment, facilities, personnel, utilities, raw material control, process risk assessment, qualification, process validation, cleaning validation, preventive maintenance, cleaning & disinfection, outsourced activities, vendor approval, monitoring system, continuous improvement, quality management system, and laboratory controls. As part of the summary and conclusion, the CCS report concluded that all required procedural controls for the processing, cleaning, movement, analysis, monitoring, qualification, and validation are available and regularly qualified.

Batch release and raw material release were reviewed during the inspection. The SOP was applicable for batch release of finished products (API)/intermediates and semi-finished products (recovered solvent/substance) after reviewing all the manufacturing and analytical records. The API release process was conducted using the SAP system, but the final release for the intermediate was conducted manually. The batch release was performed by Head QAD/Designee-QAD. The Head/Deputy -QAD verified the analytical and process data of the product and ensured to intimate agencies about the below cases before dispatch (but not limited): reprocess batch, usage of recovered solvent, rework batch, modified process, any changes in vendor, types of batches like trial, validation etc. A list of designees QAD was available and approved by the Head QA, consisting of the Head QAD and Deputy QAD.

Deviation handling had been implemented according to the SOP for event management. The SOP was applicable for initiating, reviewing, approving, and closing event records (incident and investigation) in TrackWise. The SOP covered impact assessment for batches released in the past and ongoing batches (batch impacted and subsequent batches). Deviations could be classified into three categories, i.e., minor (there was no impact on critical quality attributes/CQA), major (there was an impact on CQA, critical process parameter/CPP, etc.), and critical (there was an impact on CQA, CPP, and product quality). The flow process of deviation handling consisted of the originator reporting the event and initiating the event through TrackWise within one business day, initial review by the Head of Department/HOD, QA review, corporate QA review, event categorization (incident or investigation), root cause, CAPA, CAPA monitoring/CAPA effectiveness.

The SOP for handling corrective and preventive actions/CAPA was in place. CAPA was required due to multiple events such as OOS, OOT, incident, consumer complaint, recall, APQR, regulatory inspection, customer audit, process or system improvement, trend analysis, validation/qualification activities, quality review meetings, and QRM. The proposed CAPA that required changes was handled as per SOP on the change management system. The CAPA system was managed using the TrackWise system. The target date for the completion of CAPA was not more than 60 calendar days from the date of initiation. For any physical/mechanical changes/creation, the target date for the

completion of CAPA was not more than 180 calendar days from the date of initiation. If the CAPA action was required to be completed earlier based on the criticality, the target CAPA should be made accordingly. CAPA implementation date extension should be requested for approval from QA with a rational justification, including an impact assessment. The Site QA Head approved the first and second extensions by Corporate QA. SOP also covered the monitoring of CAPA effectiveness. Trend analysis of CAPA was conducted annually.

The system for management review was available as per SOP on quality management review. The SOP regulated the review of QMS implementation in the company, consisting of change control, incident, event, customer complaints, OOS/OOT, product recall, PQR, batch release, reprocess/rework, validation, technology transfer, regulatory update, etc. Management review at the corporate level was conducted every three months, while at the site level, it was performed every month. The latest site management review was conducted on 07/10/2024. CAPA was initiated and monitored as an action resulting from a management review.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

2. Personnel

There were 539 employees in different departments, and around 300 contractual workers (for support functions). In general, the job descriptions of the personnel were in place. A review was conducted for the job descriptions of the Site QA Head, QC Head, and Head of Manufacturing/Plant Head as key company personnel.

Personnel training was implemented according to the SOP on the training program flow chart. The SOP described the training flow from new hire/transfer employee induction, training implementation, training evaluation, OJT/on-the-job training, and training effectiveness check until annual mandatory training as per the planner. SOP for the training program through PLMS and the manual system was in place. The training program was recorded and managed on the PLMS version 2.0.0. software. Contract employees were also included in the system. The department training coordinator was responsible for implementing the training program for all departments. The training module was applied to the software. Mandatory training for all employees covered cGMP, data integrity, and safety; cGMP and safety were mandatory training for contract staff; and GLP was mandatory for QC staff. The training record of contract staff was spot-checked and found well documented. The training for all employees was conducted annually.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

3. Buildings and facilities

The building and facilities were designed and constructed to facilitate cleaning, maintenance, and operations for the types and stages of KSM, intermediates, and APIs. Overall, the entire facility was divided into the following buildings and areas:

- Block A (KSM and intermediates) (Rifapentine Stage-I)
- Block B (under construction, API, and intermediates)
- Block C Solvent Recovery Plant (SRP)
- Block D (for APIs and intermediate, Rifampicin, Levofloxacin)
- Block E & F (under construction and used for fermentation up and downstream)
- The separate building consists of a warehouse, QC, and QA

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

4. Process equipment

The list of manufacturing equipment was maintained as part of the VMP, indicating equipment name, ID, size/capacity, and location. For Block D, the following equipment and instruments were available:

a) GLR (8), qualified in Aug/Sep 2024
b) SSR (13), qualified in Aug/Sep 2024
c) Centrifuge (12), qualified in Aug/Sep 2024
d) VTD (6), qualified in Aug-Oct 2024
e) Tray dryer (1), qualified in August 2024
f) Rotary Cone dryers (5), qualified in Aug-Oct 2024
g) Multimill (6), qualified in Aug-Oct 2024
h) Vibro sifter (4), qualified in Aug-Oct 2024
i) Jet mill (1), qualified in Sept 2024

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

5. Documentation and records

The company informed that corporate SOPs are available for quality systems operated using TrackWise, whereas site-specific SOPs are available for the rest of the quality systems. A master list of SOPs was in place, according to the SOP, and was reviewed and approved by the site QA head. The following SOPs were managed on the master list of SOPs consisting of SOPs for corporate quality assurance department (71 SOPs), QA department (43 SOPs), QC department (85 SOPs), microbiology department (57 SOPs), manufacturing department (81 SOPs), engineering department (110 SOPs), health- safety and environment department (33 SOPs), warehouse department (39 SOPs), human resources department (17 SOPs), IT department (7 SOPs), and corporate IT department 114 SOPs).

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

6. Materials management

Vendor qualification and approval for the drug substance manufacturing site were reviewed. The procedure was applied to APIs. It was noted that all the suppliers of intermediates were 100% audited as part of the supplier qualification. Recommendations from the CRD/regulatory department were considered before auditing the KSM. The qualified vendors were reassessed every 5 years, and performance evaluation was performed on vendors based on the supply history.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

7. Production and in-process controls

Rifampicin was manufactured using a one-stage process wherein the route of synthesis was divided into Stages 1A, 1B, and Rifampicin. The synthesis was carried out on the top floor, wherein crystallization and powder processing were performed in the classified areas. The synthesis and powder processing areas were equipped with various equipment such as stainless-steel reactors, nutch filters, sparkle filters, centrifuges, rotacone dryers, vibro sifter, and multimill. The packing of Rifampicin was carried out in a cleanroom using the blue HDPE containers. Triple-laminated double polythene bags were used to pack Rifampicin in the HDPE containers. Silica gel and oxygen burster were placed inside the container to ensure no degradation of Rifampicin due to potential oxidation. The vacuum nitrogen sealing machine was used for packing purposes.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

8. Packaging and identification labelling of APIs and intermediates

The API packaging was performed in the powder processing area, classified as ISO 8. The packaging materials were received through a dynamic passbox, and the packed APIs were transferred to the storage area through a separate passbox. For more details, refer to Section 7 on production and in-process controls.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

9. Storage and distribution

The warehouse was visited and found adequate. Warehouse management was managed using an SAP system that covered receiving, storage, dispensing, and dispatch activities. Overall, provisions for incoming materials, intermediates, and finished products were in place for reception, quarantine, and release processes. Appropriate storage conditions were provided. procedures for handling rejected and returned materials were in place. All vendors for raw and packaging materials, including KSM (key starting material), were approved and covered on the SAP system. A logbook for weighing and sampling activities was available, and the activities were recorded adequately. Raw labels were

stored in the warehouse and printed in the production area. There was no distribution activity during the inspection, but the system was established on SAP.

10. Laboratory controls

The inspectors visited the QC laboratory on the first floor of the warehouse/QC/QA building. The samples were received and logged in physical logbooks, whereas LIMS was used to log intermediates and water analysis samples. The laboratory was equipped with 16 HPLC (Thermo Scientific and Shimadzu), 4 GC with Headspace, FTIR, UV-VIS etc. Chromeleon 7.2 was used for the chromatographic data system. The laboratory has three balances (semi-micro, micro, and ultra-micro) to support chromatographic analysis. The standard weights (E2 Grade) were calibrated once every year, and a calibration certificate was available. The balances were verified daily and calibrated monthly. Milli-Q water was used for the chromatographic analysis, whereas purified water was used for the rest of the testing. A separate water system was provided for the laboratory. pH and conductivity were tested daily. Two 2-8°C chambers were used for storing working standards and samples. The working standards for Rifampicin, Rifampicin Stage 1, Rifampicin Quinone, Rifamycin S, and Rifapentine Stage 1 were stored in the chamber.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

11. Validation

The validation master plan (VMP) provided a high-level overview and philosophy of the validation activities carried out on-site.

Analytical method validation

Related substances and assays were performed following Ph. Eur.; hence, analytical verification was performed at the laboratory level. The analytical method verification report for the determination of related substances of Rifampicin by HPLC was reviewed. The verification included specificity, solution stability, mobile phase stability, LOD, LOQ, linearity, range, precision (repeatability, intermediate precision), accuracy, relative response factor, system suitability etc. The results were found within predefined acceptance criteria.

Cleaning validation for Rifampicin was scheduled to start from Rifampicin batch number 3 onwards. The first batch has been completed, whereas 2nd and third are ongoing. Cleaning validation for Levofloxacin has been completed, and an interim report has been prepared. The SOP for cleaning validation was in place as per the document. The SOP covered key starting material (KSM) cleaning activities and intermediate and active pharmaceutical ingredients (API) facilities. The cleaning activities included cleaning process validation, cleaning verification, and periodic cleaning. There were two types of cleaning: type-I cleaning, “cleaning conducted after batch to batch,” and type-II cleaning, “cleaning after product changeover/periodic.” Periodic cleaning was defined on the SOP as the maximum allowable number of batches of the same product with the same stage manufactured before full cleaning (type-II), specifying maximum campaign lengths in 10 batches. A grouping or matrixing approach was used for cleaning validation. The flow of cleaning validation covered cleaning process design, validation/qualification, continued cleaning process verification, post-validation monitoring or cleaning verification, change control, and periodic management review. The cleaning procedure was designed to consider several parameters such as cleaning solvent, therapeutic

daily dose (TDD), permitted daily exposure (PDE), and maximum allowable carryover (MACO). Testing parameters for type I cleaning comprised a visual test only, and for type II cleaning included visual, chemical residue, impurity (whenever applicable), and microbial limit. Trending of the cleaning verification was conducted every 30 cleaning times.

Process validation

The SOP on process validation was reviewed during the inspection. It was noted that process validation involved process design—stage 1, process qualification—stage 2, and continued process verification—stage 3. For the process performance qualification (PPQ)—stage 2, the company applied prospective process validation and a concurrent process validation approach; for Rifampicin, it used a prospective approach.

Computerized system validation

The computerized system was managed per SOP on preparing and numbering of the computerized system validation and SOP on computerized system validation. The system applied by the company included enterprise application software (TrackWise, DMS, LIMS, etc.); QC laboratory application/software (Chromeleon, Labsolution, Tiamo, etc.); manufacturing process control system (SCADA, DAS, IPC, PLC-based HMI); etc. The V model approach was used on the computerized system validation by considering the GAMP 5 category and complexity, including URS, FRS, IQ, OQ, and PQ. Seven phases of the system life cycle were also considered, covering phase I (project initiation phase), phase II (requirements and planning phase), phase III (design/configuration phase), phase IV (qualification/test phase), phase V (implementation phase), phase VI (operational/maintenance phase), and phase VII (retirement phase).

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

12. Change control

The SOP for the change management system was reviewed. It noted that change controls were managed through TrackWise, whereas the SOP was managed through the document control system (DCS). The procedure was applied to APIs, FPPs, and other products handled on-site. It also applied to new product introductions, applicable GMP changes, etc. The procedure described the responsibilities, definitions, and procedures for managing changes. A cross-functional team reviewed the proposed changes before approval. The risk assessment was performed before approval of the proposed change. The effectiveness check was carried out using TrackWise. Change controls were managed manually if there was any breakdown in the TrackWise. A total of 184 changes were raised in 2024, which were classified into closed (116, critical (0), major (43), and minor (73), whereas from the open change controls (68, no critical, 38 major, 29, and one not categorized). It was noted that Rifampicin and Levofloxacin were introduced in 2024 in Block D. Change control was raised for the introduction of Rifampicin. The change was proposed based on the process development initially performed by the company's R&D in Mumbai before three batches were taken at the Sarigram site. The change control was raised to prepare the Master Production & Control Record (MPCR) and BPCR, and the change was classified as major.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

13. Rejection and re-use of materials

The SOP for reprocessing, rework, and re-distillation was reviewed. This document guided the management of reprocessing, reworking, and recovery of the finished product, intermediates, and recovered material/solvent. The procedure described various terms under definitions and was supported with examples. A unique numbering was assigned to reprocessing and reworking, and evaluation was performed beforehand. The company confirmed that solvents were recovered on-site, and no outsourcing activity was used to recover solvents and materials.

The procedure for blending batches was reviewed, and it was noted that this was the first version of the SOP. It provided guidance about the blending process, including do's and don'ts. A unique batch number was assigned as per the batch numbering procedure. The company did not perform any blending activities for APIs and intermediates.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

14. Complaints and recalls

A written procedure was established for handling customer complaints. The procedure covered information about the customer, the investigation process, and the proposed action/CAPA to prevent the defect from recurring. A product recall procedure was available as per the procedure. The SOP described information regarding product defects, the investigation process, a mock recall to ensure the recall's effectiveness, reporting to the regulatory body, etc.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

15. Contract manufacturers (including laboratories)

The manufacturer confirmed that no contract manufacturing was carried out for any of the WHO products. For testing purposes, the manufacturer sent samples to various laboratories, including its own site located in Sarigram. Some tests for Rifampicin, Rifamycin S, Levofloxacin, and Rifapentine stage-1 were only contracted out at Macleods Pharmaceuticals Ltd, Sarigram Unit – V.

The deficiencies raised in this section have been adequately addressed and 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, ***Macleods Pharmaceuticals Limited***, located at ***Plot No. D-3/27, GIDC Dahej-III, Village: Sambheti, District: Bharuch, State: Gujarat, PIN: 392130, India*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines for APIs.

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 GMP Guidelines referenced in the inspection report

1. 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/

2. 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/

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.
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