World Health Organization

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

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

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**Cipla Limited**
Corporate address of the manufacturer	**Cipla Limited** Cipla House, Peninsula Business Park, Ganpatrao Kadam Marg, Lower Parel, Mumbai - 400013, India
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Cipla Limited Plot No. 9 & 10, Pharma Zone, Phase-II, Indore SEZ, Pithampur, District Dhar, MP, India
Unit/block/ workshop number	Unit I (oral liquid dosage form) Unit IV (oral solid dosage form)
Inspection details	
Dates of inspection	12-16 June 2023
Type of inspection	Routine GMP inspection
Introduction	
Brief description of the manufacturing activities	Cipla Ltd, Pithampur is situated at Indore Special Economic Zone (SEZ) at Pithampur, Dist. Dhar, (Madhya Pradesh). It is approximately 40 kilometres from Indore city. Pithampur is a major industrial town of Madhya Pradesh home to major companies including Pharmaceutical, Textile and automotive. The Pithampur SEZ includes manufacturing units of major pharmaceutical firms.
General information about the company and site	Cipla is a public limited company established in 1935 by Dr K.A. Hamied and is managed by a professional board of directors. It has its own management control and operation and has no parent company. The Corporate Headquarters is in Mumbai including the Corporate Quality Assurance. Senior personnel are available in Mumbai to provide support to the Manufacturing units in the areas of Technology, Integrated Product Development (IPD), Manufacturing, Quality Assurance, Quality Control and Regulatory Affairs. Cipla has 8 manufacturing facilities in India: ▪ Active Pharmaceutical Ingredients are manufactured at Bengaluru, Bommasandra, Patalganga and Kurkumbh. ▪ Pharmaceutical formulations are manufactured at Indore, Goa, Patalganga, Kurkumbh, Baddi, and Sikkim.

	▪ Overseas Manufacturing sites are located at New York (USA), Massachusetts (USA); Kampala (Uganda), Durban (South Africa), Johannesburg (South Africa), and Morocco (North Africa).
History	The manufacturing site (Unit I and II) was last inspected by the WHO PQ inspection services in October 2017. In addition, Units I and IV were inspected by the WHO PQ in 2014 and 2011. The following regulatory authorities inspected the site: - USFDA – GMP Inspection 6th Feb – 17th Feb 2023 EIR awaited. See the summary of the impact assessment performed by Cipla Indore on the USFDA inspection, under Part 2 (Summary of findings and comments) in this report. - Joint Inspection by Central Drugs Standard Control Organization (CDSCO), Indore; and State Licensing Authority Controller of Food and Drug Administration, Bhopal, Madhya Pradesh, 29th to 30th Mar 2022, approved - Egypt MoH, 14th to 17th Mar 2022, approved - Brazilian Health Regulatory Agency–ANVISA, (Desk Assessment), Jan 2023, Unit IV, approved - Rwanda Food and Drugs Authority (Desk Assessment), 28th Jan. 2022, approved.
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 and materials - Production and packaging (Unit I and IV) - Quality control laboratory (Unit I and IV) - Utilities
Restrictions	None
Out of scope	The scope of the inspection was limited to the products submitted for the WHO Prequalification Program manufactured in Units I and IV. The rest of the products and their related areas were out of the scope of this inspection.
WHO products covered by the inspection	1) HA200 Nevirapine Suspension, Oral 50mg/5mL 2) MA064 Artemether/Lumefantrine Tablet 20mg/120mg 3) HA060 Lamivudine/Zidovudine Tablet, Film-coated 150mg/300mg 4) TB321 Linezolid Tablet, Film-coated 600mg 5) HA680 Dolutegravir (sodium) Tablet, Film-coated 50mg 6) MA115 Artemether/Lumefantrine Tablet, Dispersible 20mg/120mg 7) HA662 Abacavir (sulfate)/Lamivudine Tablet, Dispersible 120mg/60mg 8) NT005 Albendazole Tablet 400mg 9) HA779 Abacavir (sulfate)/ Dolutegravir (sodium)/Lamivudine Tablet, Dispersible 60 mg/5 mg/30 mg (under assessment)

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
IQ	Installation qualification
LAF	Laminar airflow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MFT	Media fill Test
MR	Management review
NC	Non-conformity
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 (where applicable)**

1. Pharmaceutical quality system

The site had a formal, documented quality system that met the requirements of the current WHO GMP Guidelines. The QA and production departments were independent of each other. The Head Site Quality and Vice President - Site Head independently reported (functionally and administratively) to the Senior Vice President Cluster Head Formulation. The site policies and procedures that were reviewed and discussed during the inspection were generally satisfactory. Product and processes were monitored, and results were considered during batch release. The following major software applications were used at the site:

Software	**Implementation Date (At Site)**	**Function**
Chromeleon System	Feb 2010	Management of Chromatographic Data
Building Management System	Sep 2011	Control and Monitoring of Environmental Conditions
System, Application and Product (SAP)	Nov 2014	Control of Batch Documents; Batch Release, Material Management etc.
Documentum System (CipDox)	July 2015	Change Management, Document Insurance etc.
Track & Trace System	Oct 2016	Serialization for Unique Verifiable Product Identifier
Laboratory Information Management System (LIMS)	April 2016	Analytical Data Management
TrackWise System	July 2017	Management of QMS Elements Viz. Deviations, CAPA, Complaints.

	July 2020	Investigation of OOS, Incidence and OOT
Learning Management System (LMS)	Jan 2020	Management of Training
e-Track	July 2021	Material Management

The following quality system elements were reviewed:

Annual product quality review (APQR)
APQR was discussed. The APQR procedure was prepared by the corporate Cipla, and it was issued through Cipdox. APQRs were prepared by QA based on the first anniversary from the start of the first commercial batch or as per customer requirements. APQR was prepared considering all batches manufactured, irrespective of the number of batches in the current year. If the number of batches are less than 10, then batches manufactured in the previous year are considered. Process capability index (Ppk) calculations were performed yearly, semi-annual, or quarterly by statisticians at the Cipla Corporate Office considering a minimum of 15 batches. If the Ppk value is ≥1.33 = high performance, if the Ppk value < 1.33 = adequate or low performance depending on the results of the stability statistical evaluation and determined to have no chance of stability failure.

Change control
SOP for change control was discussed. Changes were categorized as Major, Moderate and Minor. Major changes required risk assessment to be performed as per SOP.

Deviation and root cause analysis
The Deviation and the report were discussed. Deviations were managed in the TrackWise system as per SOP for the Deviation handling. Deviations were classified as critical, major or minor. A risk matrix was available where risk score -Impact (severity) of 1, 2 and 3 can be given. Also, a table for risk classification for likelihood was provided for scores of 1, 2 and 3. Risk numbers 1-2 were rated Minor, 3-4 rated Major, and 6-9 rated critical.

Quality risk management
The Risk management by failure mode, effects and criticality analysis procedure was discussed. A flow diagram of FMECA was part of the procedure. The procedure described the methodology to carry out a risk assessment using RPN. An FMECA log for Unit IV for 2023 was available. The existing procedure was limited to the use of FMECA. Other tools such as FTA, FMEA, Risk ranking and filtering and more were not part of the procedure. It was noted that a separate procedure was in place for handling risks related to safety (HAZOP). Upon review of the risk register, it was noted that most of the risks were related to deviations while some of the risks were related to the introduction of new equipment, change of frequency, etc.

FMECA log for Unit I for July 2022-2023 was available. Several risk assessments were carried out following the recording of deviations including the use of new equipment. The FMECA subject in the risk log was found inadequate as the description did not provide the exact nature of the risk reviewed e.g. reduction of in-process samples of vacuum leak test bottles from 27 bottles. For Unit I, no new product was introduced from July 2022 until June 2023.

Data integrity risk assessment (DIRA)

The FMECA for breach of data integrity on the electronic data was discussed. The potential failure mode e.g., breach of DI of the electronic data was identified and accordingly, potential effects or consequences were identified. The risk assessment document identified current control measures such as SOPs on validation of the computerized system, incident management, qualification of equipment, security in electronic data, review of audit trail, backup and restoration, retention and destruction of electronic data and many other procedures. This FMECA was generic for all electronic data.

Excipient risk assessment

The Risk assessment for the excipients used in the finished product was evaluated and noted that excipient manufacturers were assessed following the IPEC guideline (instead of European Directives and PIC/S).

New product introduction

The SOP on the allocation of a manufacturing site for a new product was discussed. Allocation of the manufacturing site for a new product was initiated through Cipla Vikhroli. The FMECA initial calculus was performed and confirmed that all controls were adequate hence no additional controls were required. Another FMECA (RPN score) was performed to determine contributory factors. Some action plans were identified and were to be followed up through change control/TrackWise.

Antimicrobial resistance stewardship and site risk assessment

The company identified five products as antimicrobials: Ciprofloxacin, Levofloxacin, Fosfomycin, Linezolid and Nitrofurantoin. The waste was broadly handled as solid and liquid waste. Solid waste was handled through incineration whereas liquid waste was handled through reverse osmosis and as such it was regarded as a zero-discharge site. The company followed AMR industry alliance antibiotic discharge targets (list of Predicted No-Effect Concentrations [PNECs]) and performed testing on the discharge levels for the materials. Upon review of some of the certificates of analysis for Ciprofloxacin and Levofloxacin, the results were reported well below the limit of quantitation. In addition, the company performed FMECA for antimicrobial resistance to the environment and confirmed that the current controls were adequate concerning AMR. A draft SOP from the corporate office was in place for handling waste management.

Management review

The Quality Management Review was checked. According to the organizational structure (dated 9/06/2023), the Head of Site Quality and the Site Head both constitute Senior Management as per the definition in the Corporate SOP. Management review meetings were required to be held monthly. The management review report was presented. The meeting attended by 15 out of the 20 members was reviewed and discussed. The Site Head (the most responsible person on Site) and the Head of Site Quality were present, and both signed the report. Other monthly reports seen were consistent with the SOP. Actions for improvement require the provision of resources that were approved by senior management.

The deficiencies were addressed satisfactorily and the same will be verified during future PQ inspections.

2. Good manufacturing practices for pharmaceutical products

Cipla Limited, Unit I (oral liquids) & Unit IV (oral solid dosage form) is a facility manufacturing pharmaceutical products of different therapeutic categories. Most of the operations were carried out in closed systems using vacuum transfer systems for granules in Unit IV and stainless-steel transfer pipes for the liquid oral preparations in Unit I. Basic principles of good manufacturing practices were defined in standard operating procedures. Manufacturing and packaging steps were adequately defined in batch manufacturing records and batch packaging records. The storage and distribution of products ensured batch traceability from receiving to final product and testing. Required resources were available, including adequate premises, equipment, and utilities. Appropriately qualified personnel were employed, and in general, training was performed. Qualification and validation were performed following approved protocols.

Access to the oral solid dosage manufacturing area was via an electronic access control system. Separate entries were available for men, women and visitors. Primary and secondary gowning was observed before entry into the manufacturing area and tertiary gowning to access dispensing areas.

The deficiencies were addressed satisfactorily and the same will be verified during future PQ inspections.

3. Sanitation and hygiene

A considerable good degree of sanitation and hygiene was in place from the changing room to the manufacturing floor and the packaging of the final product. The personnel were provided with appropriate gowning at each activity area commensurate with the level of cleanliness. Production equipment were in a clean state, and cleaning procedures for equipment were in place. Containers used for transporting raw dispensed and in-process materials were clean and covered. Production materials were appropriately stored to avoid contamination and cross-contamination. The facility was generally in an acceptable state of cleanliness at the time of inspection.

The deficiencies were addressed satisfactorily and the same will be verified during future PQ inspections.

4. Qualification and validation

The validation master plan provided an overview of the validation activities and responsibilities. The following validation activities were reviewed:

Cleaning validation and establishment of the worst-case product were discussed. Solubility, potency and toxicity were taken to determine the worst case whereas three criteria were established (dose criteria, 10ppm criteria and PDE criteria) for cleaning validation.

Process validation SOP was discussed and noted that a three-stage concept was followed to validate the process. Stage 1 is carried out at Cipla's R&D (integrated process development) located in Mumbai. The process development report has been requested. For Stage 2, it was stated that at least 3 consecutive batches shall be validated.

The deficiencies were addressed satisfactorily and the same will be verified during future PQ inspections.

5. Complaints

The SOP on Handling of Product Complaints was reviewed. Complaints were classified as Critical or non-critical. Investigations were required and root cause analysis was performed as per SOP. Receipt of a complaint had to be acknowledged within one working day. Feedback for the complaints: timelines for complaint processing were indicated and depended on whether the complaint was critical or non-critical. Critical had to be addressed within one working day, while non-critical complaints within 30 working days. Close-out for both categories of complaints was within 60 days of logging in of a complaint.

The deficiencies were addressed satisfactorily and the same will be verified during future PQ inspections.

6. Product recalls

There have been no product recalls in the last three years.

7. Contract production, analysis and other activities

The company management confirmed that no part of the manufacturing was contracted out for any of the WHO-prequalified and under-assessment products. Some of the laboratory tests are carried out by the contracted laboratories, e.g. nitrosamine impurities in finished products. Some of the tests in excipients were also outsourced.

The deficiencies were addressed satisfactorily and the same will be verified during future PQ inspections.

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

The SOP on Internal Audit was discussed. The frequency of the audits was determined by risk category and compliance level (in terms of "good", "satisfactory" and "need attention") and it was carried out within six months. Training and certification of auditors were described in the SOP and required training of personnel followed by certification through observed inspections and meeting the requirements for education, training and experience. The list of certified internal auditors included 16 certified auditors (digitally signed on 17.01.2023), and one certified auditor on the list dated 19.04.2023, approved by the Audits and Compliance department. The audit schedule for the period January to December 2023 was discussed.

A list of qualified vendors for APIs, excipients, and packaging materials, prepared product-wise, shows the name and address of the manufacturers and validity of the manufacturer and validity of the TSE/BSE certificate, managed in the SAP system.

The deficiencies were addressed satisfactorily and the same will be verified during future PQ inspections.

9. Personnel

There were organograms available for the site and other functional departments to ensure that reporting lines between various levels of management, heads of the various departments, supervisors, and operatives were clear.

10. Training

Training of production personnel in Unit I was verified. Deputy Manager, Section Head for Unit I was required to carry out training on SOPs for manufacturing, dispensing, QMS, documentation, SAP, CipDox, and general topics and SOPs. The training had been carried out. Monitoring of the training for production persons in Unit I was carried out in LMS (Learning Management System software application).

The deficiencies were addressed satisfactorily and the same will be verified during future PQ inspections.

11. Personal hygiene

The procedure for personal hygiene was available. The personnel were required to undergo health examinations including eye check-ups. During the inspection, it was observed that an adequate level of personal hygiene was observed by the staff.

12. Premises

The total plot area of the site is about 153100 sq. m. The Unit-wise built-up area is as follows: Unit I: 26,110 m^2, Unit II: 11,213.50 m^2, Unit III: 22,545 m^2, and Unit IV: 39400 m^2. There are separate blocks for the manufacturing of different formulations. The scope of the inspection was limited to Units I and IV.

Warehouse

There were independent stores for Unit I and Unit IV. The incoming materials were visually checked for signs of damage to the containers and intactness of seals and against the relevant purchase order. Containers were cleaned before entry into the warehouse and stored as per their desired storage condition. The materials were segregated based on batch numbers and stored inside the compartment. The SAP was used to generate the SAP batch number and materials were labelled for traceability and identification and quarantined in designated areas. Sampling was performed by the QC personnel. Dispensing was performed by a designated store person and witnessed by the production personnel. The materials were dispensed on a 'First Expiry First in First Out' (FIFO) basis.

Compressed air

The SOP on condition monitoring and replacement of 1um and 0.01um compressed air/nitrogen gas filters was discussed. The schematic diagram of the compressed air system was reviewed and noted that 0.01µm was provided in the service area before compressed air was distributed to the user points. A risk assessment was performed and noted that some of the user points have having additional 0.01µm. The

pipeline of the compressed air was made of SS304. The filters were monthly verified and yearly replaced. In addition, a yearly schedule was available for the sampling and testing of compressed air.

The deficiencies were addressed satisfactorily and the same will be verified during future PQ inspections.

13. Equipment

Each Unit had its own Unit Engineering Head, with its engineering team responsible for production equipment and utilities (HVACs, chiller units, air compressors, DG sets backup, electrical panels, purified water generation systems, etc.). SOP for Equipment/System maintenance was discussed. Preventive maintenance frequency is shown in Table 10 of the SOP and shows PPM frequencies ranging from weekly, fortnightly, monthly, bimonthly, quarterly, four monthly, six monthly and yearly. The annual PPM plan and schedule were managed in SAP.

The deficiencies were addressed satisfactorily and the same will be verified during future PQ inspections.

14. Materials

The raw and packing materials were procured from approved sources. The incoming materials were visually checked for signs of damage to the containers and the intactness of the seals. The materials were stored as per their desired storage condition. The segregation was ensured as per the manufacturer's batch number. A Goods Received Note (GRN) was prepared in SAP and the SAP batch number was automatically generated. The materials were labelled for traceability and identification and quarantined in designated areas. Sampling was carried out by Quality Control personnel.

The deficiencies were addressed satisfactorily and the same will be verified during future PQ inspections.

15. Documentation

The SOP on documentation control was discussed. It guided the handling and managing of documents. The procedure guided handling documents of internal and external origins, in particular, how raw data were handled. The raw data received from external origins was verified by Cipla and the same was retained with parent documents. The procedure also guided the retention period (permanent to certain years) and the responsibility of various departments. A policy on good documentation practices and documentation control was available. The policy applied to all types of documentation i.e. paper-based, electronic or photographic media carried out across Cipla and its associate units which directly or indirectly impact all aspects of the quality of medicinal products.

SOPs in the manufacturing areas were accessed digitally (electronically) using portable hand-held computer units.

The deficiencies were addressed satisfactorily and the same will be verified during future PQ inspections.

16. Good practices in production

Most process equipment in Unit I and Unit IV had PLC/HMI controls. There were four level access controls for the HMIs. Compression machines were fully automated (Fette) with HMIs, and online metal detectors. Environment monitoring and control for temperature and humidity in the controlled areas was performed with the use of Building Management System (BMS) software with fully electric data acquisition, recording and trending of actual temperature, relative humidity and room differential pressures for each room in Unit I and Unit IV. A review of the real-time readings and trends for temperature, relative humidity and room differential pressures was carried out by a dedicated full-time operator. In-process quality controls during tablet compression were performed in each cubicle for individual tablet weight, group weight for 20 tablets, friability, and tablet dimensions. Tablet disintegration testing was carried out outside the compression cubicles in the central IPQC room.

The deficiencies were addressed satisfactorily and the same will be verified during future PQ inspections.

17. Good practices in quality control

The quality control laboratory was independent of the production department. In particular, Units I and IV have independent QC laboratories for chemical and physicochemical analysis. There were two microbiology laboratories located in Unit I and Unit III.

The QC laboratories used LabWare LIMS version 6.01H. Primary data capture from analytical balance was directly entered into LIMS, but data entry into Chromeleon 7.2.10ES used for HPLCs was carried out manually. Controlled Test Data Sheets were printed in the LIMS and there was a means of identification and traceability of subsequent printing of Test Data Sheets for the same sample in case of OOS results investigation. Samples allocation to analysts/microbiologists for testing was based on competence. The Identification of Training Needs and Competence matrix sheet dated 17 Jan 2023 was used as a reference.

The SOP on stability studies was discussed. The stability study protocols are prepared for each product, including the test type, storage conditions, quantities required for every station/time point, etc. The products for WHO markets were kept in climatic chambers maintained at 25ºC/60% RH, 30ºC /65% RH, and 30ºC /75% RH for the ongoing stability program. The pull-out window was set to three working days.

The deficiencies were 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, ***Cipla Limited***, located at ***Plot No. 9 & 10, Pharma Zone, Phase-II, Indore SEZ, Pithampur, District Dhar, MP, India*** 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-eight Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2.
   Short name: WHO TRS No. 986, Annex 2
   https://www.who.int/publications/m/item/trs986-annex2

2. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2.
   Short name: WHO TRS No. 957, Annex 2
   https://www.who.int/publications/m/item/annex-2-trs-957

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

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

5. 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
   https://www.who.int/publications/m/item/trs957-annex1

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

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

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

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

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

11. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-First Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. ***Short name: WHO TRS No. 943, Annex 3***
https://www.who.int/publications/m/item/trs943-annex3

12. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2.
Short name: WHO TRS No. 961, Annex 2
https://www.who.int/publications/m/item/trs961-annex2

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

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

15. 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
https://www.who.int/publications/m/item/tr961-annex14

16. 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://www.who.int/publications/m/item/trs1019-annex3

17. 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
https://www.who.int/publications/m/item/trs992-annex4

18. 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://www.who.int/publications/m/item/trs961-annex9-modelguidanceforstoragetransport

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
https://www.who.int/publications/m/item/trs992-annex5

20. WHO Recommendations for quality requirements when plant – derived artemisinin 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/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
https://www.who.int/publications/m/item/annex-4-trs-1033

22. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
Short name: WHO TRS No. 996, Annex 10
https://www.who.int/publications/m/item/trs966-annex10
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***
https://www.who.int/publications/m/item/trs1010-annex10

24. 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
https://www.who.int/publications/m/item/annex-2-trs-1033

25. 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
https://www.who.int/publications/m/item/trs-1025-annex-6

26. 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/m/item/trs-1025-annex-3-water-for-injection

27. 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/m/item/trs1025-annex4