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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	**Ipca Laboratories Ltd**
Corporate address of the manufacturer	Ipca Laboratories Limited, 48, Kandivli Industrial Estate, Kandivli (West) Mumbai 400 067, Maharashtra, India
Inspected site	
Name & address of inspected manufacturing site if different from that given above	89A-B, 90/91 Industrial Estate, Pologround Indore, Madhya Pradesh 452003 India D-U-N-S No.: 65-080-5471 Latitude: N 2 2 ° 7 3 . 7 9 4 ‘ Longitude: E 7 5 ° 8 5 . 5 5 6 ‘
Synthetic unit /Block/ Workshop	Amodiaquine HCl (Plant 05 and powder processing area 05) Piperaquine Phosphate (Plant 03A, 05 and powder processing area 05)
Dates of inspection	19-23 June 2023
Type of inspection	Routine GMP inspection
Introduction	
Brief description of the manufacturing activities	Ipca Laboratories Limited (Plot Numbers: 89A-B/90/91 & 78/79/80 across the public road (Opp. 89/90), Industrial State Polo-Ground Indore, Madhya Pradesh; India manufactures active pharmaceuticals ingredients and intermediates. The site has been in operation since 1994 and was taken over by the British Drug House (BDH).
General information about the company and site	Ipca Laboratories Limited is a leading pharmaceutical company with manufacturing activities in the areas of active pharmaceutical ingredients, drug intermediates and finished pharmaceutical products.
History	The WHO PQ last inspected the site in October 2019. In addition, the manufacturing site was periodically inspected by the State FDA of Madhya Pradesh and the CDSCO.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	The following areas were inspected: - Quality management - Quality risk management - Personnel and training - Equipment and materials

	- Premises and facilities - Production and packaging (Plant 03A and 05) - Quality control laboratories - Air handling units - Water system
Restrictions	None
Out of scope	This inspection focused on Amodiaquine HCl active pharmaceutical ingredient (API) and Piperaquine Phosphate API. Other APIs were out of the scope of this inspection.
WHO APIs covered by the inspection	APIMF030 (Amodiaquine Hydrochloride) APIMF227 (Piperaquine Phosphate)
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
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
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 (where applicable)**

1. Quality management

A Quality Management System (QMS) was comprised of documents, processes, procedures, and responsibilities for achieving quality policies and objectives. The QMS was based on ICH-Q7, EudraLex Part IV, CFR 21 Part 11 GMP guidelines. The quality assurance department was headed by the Deputy General Manager, QA who reported directly to the Vice President, Corporate QA.

The quality management system used the following software applications:

Software	Function
TrackWise System	Quality Management System (Deviation, CAPA, Effectiveness Check, Investigation, Change control & Product Complaints)
Supply Chain Management (SCM)	Material Management, Label Management, Batch Disposition, Stability management
Electronic Document Management System (eDMS)	Document Management system (CSOPs, Specifications, STP, GTP, SOPs, BPCR & Other QMS documents)
Learning Management System (eLMS) *(under implementation)*	Training Management System
Laboratory Information Management System (LIMS)	Sample Management

Schedule Manager	To track scheduled activity (PM, Calibration etc)
One Lab. Solution *(under implementation)*	For laboratory system management (Sampling & Analysis)
Access Management	For various Software Access Management
e-Logbook (*under implementation)*	For activity / daily data recording

Product Quality Review

Annual Product Quality Review of active pharmaceutical ingredients & intermediates was discussed. The SOP used the PQR as listed in Section 1.10 of the WHO TRS 986 Annex 2. APQR were required to be completed within 3 months from the date of completion of a year e.g. Jan to Dec. The reference used for the SOP was WHO TRS 986, 2014, Annex 2 and ICH Q7. The APQR for Amodiaquine Phosphate HCL (Q5) for the years January to December 2022 was discussed. A total of 59 batches were manufactured. Cpk specifications and interpretation, were as shown below:

Cpk >1.33 (the process is capable)
Cpk =1 to 1.33 (the process is barely capable)
Cpk <1 (process not capable)
Cpk computations were done in Minitab software, version 20. The version was recently

Quality risk management

Corporate SOP on quality risk management was discussed. The procedure guided the preparation and maintenance of risk management plans and risk evaluation and mitigation strategies (REMS). It was noted that the site had performed a risk assessment for all APIs manufactured on-site.

Handling of Deviation

The SOP guided the initiation, approval, risk evaluation, execution, tracking and closure deviations. The deviations were classified into major and minor and were handled through TrackWise software. The procedure described various tools (such as 5 Why analysis, 6M or fish-bone diagram, fault tree analysis, brainstorming, Genchi Genbutsu and root cause analysis.

Internal Audit/Self Inspection

Self-inspection SOP was discussed. The list of qualified auditors approved on 7/03/2023, contained a total of 33 auditors. Criteria for Auditor qualification were provided in the SOP. Self-inspection schedules were prepared on an annual basis. The schedule for Jan to Dec. 2023 was approved on 29/12/2022 and updated on 15/05/2023. QA person was always the team leader. An internal audit had been done and closed for the Process Chemistry Excellence (PCE) lab that was scheduled in March 2013 and carried out. A self-inspection notification letter was available for the audit. The self-inspection attendance record for the opening and closing meeting that was signed was available where 8 persons signed. The report was submitted to the Site Head on 12/04/2023 (the same date as the self-inspection report).

The deficiencies related to this section have been adequately addressed and the same will be verified during future PQ inspections.

2. Personnel

The details of the personnel who were engaged in various manufacturing activities are as follows:

Sr. No.	Department	Technical personnel	Permanent Workers	Operators	Total personnel
1	Production	91	29	101	221
2	Quality Control	52	0	8	60
3	Quality Assurance	20	0	0	20
4	Warehouse	11	0	1	12
5	Engineering	28	10	14	52
6	HR & Administration	12	1	1	14
7	EHS	11	1	3	15
8	PCE Lab.	11	0	3	14
9	Others	10	1	0	11
Total		246	42	131	419

In addition to the above personnel, the site uses contracted employees mainly for handling materials, housekeeping and for security management.

Organogram and Job Descriptions

The SOP for Organogram and job responsibility was discussed. This was a corporate SOP, previously there was a site SOP. It provided for functional and operational organograms, their preparation, review and approval. It also provided for contents of job responsibilities of employees. The approved organogram was approved by the Site Head.

Training

The SOP for training management was discussed. Job-specific training (functional training) for personnel in the QC Lab and in production Block 5 were discussed. The list of employees for QC indicated a total of 60 employees, mainly university degree graduates, with experience ranging from one year to 31 years. The SOP for training, qualification & certification of analysts & qualification of reviewers, supervisors and sampling persons was discussed. Certification of the analyst was required for 13 elements and techniques that included HPLC, IR, sampling, etc., and certification of reviewers/supervisors.

The deficiencies related to this section have been adequately addressed and the same will be verified during future PQ inspections.

3. Buildings and facilities

The buildings and facilities used in the manufacture of intermediates and APIs were located and constructed to facilitate cleaning, maintenance, and operations as appropriate to the type and stage of manufacture. The manufacturing facility/floors were designed based on the gravity/flow of the manufacturing process i.e. ground floor was designed for isolation, drying & final powder processing and above the ground floor, floors were designed for chemical reaction, isolation and drying purposes. The sizes of the different plants and areas were as follows:

Area	Area (M^2)
Plant No. – 01	373
Plant No. – 02	364
Plant No. – 03	408
Plant No. – 04	63
Plant No. – 05	218
Plant No. – 08	240
Warehouse	165
Quality Control, Microbiology lab, Stability Section & Retention sample room	109
Quality Assurance	21
Water purification plant, Utility, and Others	292

The utilities available are listed below:

Water	
Raw water sources	Municipal Corporation and bore wells
Storage tanks	Total capacity 100 + 50,000 liters
Water purification system	Ion exchange type (5 m^3/hour) followed by reverse osmosis
Air	
Compressed air	210 CFM Compressors
Nitrogen generation	1 unit (Total capacity 10 NM^3/hour)
Power	
Connected load	2,500 kVA

In general, the facility was adequately maintained.

The deficiencies related to this section have been adequately addressed and the same will be verified during future PQ inspections.

4. Process equipment

Reactors were used to carry out chemical reactions between two or more reactants. The details of the reactors used on-site are as follows:

Name of Equipment	Quantity	Capacity
Mild steel/stainless steel Reactor/ Crystallizer	66	0.5 – 7.0 KL
Glass-lined Reactor	21	0.25 – 5.0 KL
Centrifuge	17	18" – 60"
Dryer (Tray)	5	72 – 96 Trays
Rotocone Vacuum Dryer	6	1.5– 4.0 KL
Nutsch Filter	5	0.1 – 1.0 KL
Agitated Neutch Filter cum Dryer (ANFD)	4	2.5 - 5.0 KL
Sifter	7	30" – 48"
Multimill	9	100 Kg/Hr.
Air Classifier mill (ACM)	2	100 Kg/Hr. – 250 Kg/Hr.

The WHO-prequalified products were manufactured using qualified process equipment. The details of the equipment and instruments used in the quality control laboratories are discussed in section 10.

The deficiencies related to this section have been adequately addressed and the same will be verified during future PQ inspections.

5. Documentation and records

The e-DMS (electronic document management system) was used for control of corporate SOPS, specifications, standard test procedures, general test procedures, site SOPs, BPCRs, and protocols. The SOP for the handling of the e-DMS application was reviewed. SOP review frequency was three years. The corporate procedure for the preparation and issuance of raw material, packaging material, critical consumables, finished product specifications, test procedures, specific test procedures, general test procedures and code assignment for APIs and intermediates was reviewed. The procedure stated under 5.1.24 that "specifications are to be revised only if some technical or editorial change is done to the specifications and/or analytical procedures. Revisions for minor and major changes are handled through change control".

The deficiencies related to this section have been adequately addressed and the same will be verified during future PQ inspections.

6. Materials management

The SOP for receipt, storage and issue of raw materials was discussed. Supply management (SCM) software version (developed by Ipca) was used. The SOP for Supply management software "Operation of supply chain management for API and common division" was discussed which provided capabilities for

modules for Security Gate Entry, inventory management, production, QA/QC, bonded storeroom (finished goods warehouse), admin, and stability (through LIMS).

The deficiencies related to this section have been adequately addressed and the same will be verified during future PQ inspections.

7. Production and in-process controls

The inspectors visited Plant 05 used for the manufacturing of Amodiaquine HCl and Piperaquine Phosphate. At the time of the visit, Amodiaquine HCl was under manufacturing at different stages. The SSR was used for stage 1. The area was equipped with an electronic clock, temperature display and calibrated receiver. The materials were charged through a manhole. The GLR was used for crystallization and TLC was performed by QC. Crystallization was in one lot and centrifugation was performed in 4 lots. After the centrifugation, the material was transferred to the powder processing area for further processing activities. The synthesis was carried out under "controlled non-classified" (CNC) and various synthesis activities were carried out under overpressure to the respective areas. It was noted that nitrogen and/or compressed air were not used during the manufacturing process. Candle filters were used in series for IPAAC/DNS equipped with a 5µm filter. The filters were replaced once every 30 batches and it was confirmed through a status label. Dedicated centrifuge bags were used for different products. The powder processing area (PPA) was qualified to meet ISO 8 Grade. The milling, sifting and packing were carried out in the same room. At the time of the visit, no activity was being carried out in the PPA. The area was equipped with separate MAL and PAL.

The deficiencies related to this section have been adequately addressed and the same will be verified during future PQ inspections.

8. Packaging and identification labelling of APIs and intermediates

The blending of APIs and intermediates procedure was reviewed. The procedure stated that OOS batches must not be blended including reworked batches with regular batches. A checklist and requisition for the initiation of blending were used by the production personnel before blending was performed. The guidance provided in the procedure was transcribed into a checklist form. The checklist was reviewed and approved by the QA before the batch record was issued for the blended product. It was noted that the site does not perform any blending activity for the WHO PQ APIs as well as for other products manufactured on-site. The blending may be performed for key starting materials which are used for the WHO PQ APIs as finished products. A full quantity was shipped to the customers hence blending of the APIs was not applicable.

The deficiencies related to this section have been adequately addressed and the same will be verified during future PQ inspections.

9. Storage and distribution

This was managed using the Supply Management (SCM) software developed by Ipca and described in corporate SOPs. Materials were handled and stored in the warehouse in a manner that prevented potential risk of contamination and cross-contamination. The materials were stored under conditions as required and FIFO was followed.

The deficiencies related to this section have been adequately addressed and the same will be verified during future PQ inspections.

10. Laboratory controls

The quality control laboratory was equipped with equipment and instruments required to carry out testing for Amodiaquine HCl and Piperaquine Phosphate. The laboratory has 5 HPLC and 5 GC systems which were connected with Chromeleon 7.2. The QC team was comprised of analysts, microbiologists, and operators. The supervisors were responsible for reviewing the data and the laboratory QA was also responsible for reviewing the lab data. The LIMS was used to log incoming samples (raw materials and finished products) except for in-process samples and intermediates which were manually recorded in the logbook. At the time of the visit to the laboratory, no samples of Amodiaquine HCl and Piperaquine Phosphate were awaiting testing. It was noted that LIMS was implemented at the site and e-Logbook and ONE Lab software applications will be implemented in a phased manner. It was noted that the laboratory had started implementing ONE Lab software which will be interfaced with all equipment and instruments (E2E).

The microbiology laboratory was responsible for performing microbial limit tests (MLT), water testing and environmental monitoring. The MLT was performed on every 10th batch of Amodiaquine HCl and Piperaquine Phosphate and/or based on customer requirements. Growth promotion tests were performed on each dehydrated media. The preparation details were recorded in a logbook. Another logbook was used to record details of microorganisms containing details of lot number etc. The sterilization cycle chart printout and record were verified for SDA media and found adequate.

Out of specifications

The corporate SOP on out-of-specification test results was reviewed. The OOSs were handled manually whereas the e-logbook was maintained for logging purposes. The OOS were investigated in a phased manner and a hypothesis was performed to confirm obvious laboratory error by using the initially prepared solution.

Incidents or events

The handling of laboratory events was reviewed and it was noted that the procedure described laboratory events as unexpected, unplanned or unintentional events which were out of human control and occurred during the execution of analysis. The events were classified as chromatographic data system events and non-chromatographic data system-related events.

Stability Monitoring of APIs

The corporate procedure on stability studies for APIs and intermediates procedure was reviewed. The procedure stated that a minimum of one product batch should be charged for the stability study. Since the shelf-life of both APIs is 5 years, the testing interval was set to be 12, 24, 36, 48 & 60 months. The procedure also stated that samples shall be prepared for different stability intervals by using the packing material the same as the marketed pack or as per QC recommendation under a controlled area/laminar airflow/isolator. The procedure stated that samples should be withdrawn from the chamber within one working day from the due date for all three conditions. Similarly, the procedure described that analysis

should be completed within 15 and 30 days for accelerated and long-term/intermediate conditions respectively.

The deficiencies related to this section have been adequately addressed and the same will be verified during future PQ inspections.

11. Validation

The validation master plan for 2023 provided guidance on validation activities for processes and systems used across the manufacturing site. The process validation was carried out by taking at least three batches of the products. It was confirmed that process validation for both Amodiaquine HCl and Piperazine Phosphate (both performed in 2020) was performed and no changes have been made since then.

Cleaning Validation

The corporate SOP for cleaning validation for APIs and intermediates was discussed. It was noted that the procedure referred to four approaches to be adopted for cleaning validation e.g. PDE, the therapeutic daily dose (TDD), 10ppm, and LD50. Cleaning validation for Amodiaquine was performed in December 2019 and was reviewed and noted that MACO was calculated using 10ppm, TDD and PDE approach. The lowest MACO was arrived from 10ppm criteria and was found to be stringent compared to TDD and PDE. An addendum to the cleaning validation of Amodiaquine HCl was discussed. It was noted that the site stopped manufacturing Primaquine Phosphate and Amodiaquine from Plant 05 dated 23/05/2023. It was also noted that the first and last campaign of Primaquine was taken in 2018 whereas Amodiaquine was last manufactured in 2019. Currently, there are only two APIs namely Amodiaquine HCl and Piperaquine Phosphate are being manufactured in Plant 05.

Qualification of Processing Areas

Block 5 schematic for dry powder processing areas (PPA) was discussed. The area included a rotary drying centrifuge process, drying in a rotary dryer, sieving, milling and sieving, primary packaging in LDPE clear bags, and secondary packing in HDPE. One AHU used for PPA used for processing of three products: amodiaquine, piperaquine phosphate and primaquine. Recently primaquine processing was discontinued due to very low demand. The PPA areas are classified as ISO 8. The wet processing areas have separate AHUs. Monitoring of room temperature, relative humidity and differential pressures done manually.

The deficiencies related to this section have been adequately addressed and the same will be verified during future PQ inspections.

12. Change control

The corporate SOP on the procedure for change control proposal for API and intermediates was discussed. It is a mandatory corporate SOP wherein the site was required to implement the said procedure without developing a site-level SOP. Changes were handled through TrackWise and were classified into major and minor. A technical committee review was required when changes were classified as major. As per the procedure, change controls should be closed within 90 calendar days whereas two extensions are allowed. In 2023, a total of 102 changes were raised whereas 95 changes were still open. In 2022, a total of 207 changes were raised whereas 46 changes were classified as major and the rest as minor. A total of 20 changes were still open.

The deficiencies related to this section have been adequately addressed and the same will be verified during future PQ inspections.

13. Rejection and re-use of materials

Reprocessing and reworking of API and intermediates were reviewed. The procedure described what is meant by reprocessing and reworking and both were handled through a detailed assessment. The procedure stated that reprocessed and reworked batches would only be allocated to the regulated markets where the reprocessing procedure was submitted and approved by the respective authority. In the case of WHO PQ, no reprocessing and reworking were part of the DMF. The proposal for reprocessing required QA assessment on the use of the reprocessing method based on R&D inputs and whether stability studies and validation are required or not. Similarly, reworking was handled through an assessment by QA based on the inputs from R&D.

The site-specific procedure for the movement of fresh and distilled solvents in plant number 05 was discussed. This procedure was limited to the recovery of solvents for Amodiaquine HCl and Piperaquine Phosphate. The site has specific solvent recovery procedures for different plants. For Amodiaquine HCl, DNS was recovered on-site. For Piperaquine Phosphate, Toluene and denatured spirit (DNS) were recovered.

The deficiencies related to this section have been adequately addressed and the same will be verified during future PQ inspections.

14. Complaints and recalls

Handling of product complaints for API and finished intermediates was discussed. The complaints were handled through TrackWise since mid-2022. All complaints related to products were received by the marketing manager whereas other complaints related to regulatory agencies go to the CQA. The internal complaints within Ipca were handled by the CQA coordinator. The complaints were categorized into critical, major and minor and timelines were specified including the closure of the complaints. A process flow chart was part of the procedure. Various SOPs related to the investigation procedure, recall of APIs and intermediates etc were cross-referenced in the complaint procedure.

<u>Product recall</u>
The SOP for the recall of APIs and intermediates was discussed. It was noted that QA was responsible for making a recall committee whereas the company's managing director was responsible for recalling APIs and intermediates. The recalls were classified into Class I, II and III. A timeline of 24 hours and 48 hours was set for Class I and II recalls.

The procedure also stated performing mock recall once every year. The last mock recall was performed in January 2023 following a protocol-based study. Primaquine Phosphate was taken to demonstrate recall system effectiveness. As per the policy, the mock recall was required to be performed on a batch supplied one year ago and an initiation form duly signed by the managing director was sent to domestic (India) and overseas (Indonesia) customers. The customers confirmed the receipt of the initiation form along with the quantity available to them.

The deficiencies related to this section have been adequately addressed and the same will be verified during future PQ inspections.

15. Contract manufacturers (including laboratories)

The company confirmed that there was no contract manufacturing carried out for WHO PQ products except testing of some tests. The SOP for vendor qualification was discussed. The SOP requires desk assessment of information obtained from the vendor before an on-site audit would be considered.

The deficiencies related to this section have been adequately addressed 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, ***Ipca Laboratories Ltd.,*** located at ***89A-B, 90/91 Industrial Estate, Pologround, Indore, Madhya Pradesh 452003, 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 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 technology transfer 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.
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