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

Part 1	**General information**
Manufacturers details	
Name of manufacturer	IPCA Laboratories Limited
Corporate address of manufacturer	48, Kandivli Industrial Estate, Kandivli (west) Mumbai 400067, Maharashtra, lndia
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Ipca Laboratories Limited (Indore) 89 A-B/90/91 & 78/79/80 across the public road (Opp.89/90), Industrial Estate Polo-ground Indore-452003, Madhya Pradesh, India
Synthetic unit /Block/ Workshop	Plant 1: Micronizing for APIs Plant 3: intermediate for Piperaquine phosphate Plant 5: Piperaquine Phosphate & Amodiaquine Hydrochloride PPA 06: Drying for Intermediates
Inspection details	
Dates of inspection	14-17 October 2019
Type of inspection	Routine inspection
Introduction	
Brief description of the manufacturing activities	Manufacturing and quality control of APIs and intermediates.
General information about the company and site	Ipca Laboratories Limited (Indore) was established in 1994. The site located in Indore, India. There were several production buildings as well as some buildings housing utilities, warehouse, administration and quality control. There were no penicillin and other β-lactam products, cytotoxic or other high potent materials manufactured on this site. 409 people were employed by the company at the time of inspection. Note: Amodiaquine HCL (APIMF30) was also manufactured by Ipca Ratlam site. The letter J represented Indore, I represented Ratlam.
History	This was the fifth WHO PQ inspection at this site. The previous WHO inspection was carried out from 29 February to 3rd March 2016. The site has not been inspected by any other foreign NRAs.

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	The inspection covered the following areas: ▪ Quality management system ▪ Personnel ▪ Buildings and facilities ▪ Process equipment ▪ Documentation and records ▪ Materials management ▪ Production and in-process controls ▪ Packaging and identification labelling of APIs and intermediates ▪ Storage and distribution ▪ Laboratory controls ▪ Validation ▪ Change control ▪ Rejection and reuse of materials ▪ Complaints and recalls ▪ Contract manufacturers (including laboratories) ▪ Implementation of CAPAs as result if the previous WHO inspection **Site areas visited:** ▪Plant 1, 3, 5 and PPA06 ▪QC laboratories ▪Warehouses ▪Water system ▪HVAC system
Restrictions	Other products and/or processes outside of WHO pre-qualification were not inspected during this inspection.
Out of scope	API products or intermediates other than Amodiaquine hydrochloride (APIMF030) or Piperaquine phosphate (APIMF227) manufactured on this site were outside the scope of this inspection.
WHO APIs covered by the inspection	Amodiaquine hydrochloride (APIMF030) Piperaquine phosphate (APIMF227)
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	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
RH	Relative humidity
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 formal documented system of quality management was generally established with procedures covering key quality elements being in place. The quality management procedures were divided into corporate and site levels. The quality Unit was independent of production. Product and process were monitored. A specified person was responsible for batch release of finished APIs products. The procedures that were reviewed and discussed during the inspection.

Product quality review (PQR)

PQRs were performed annually according to the SOP "Annual Product Quality Review of API &intermediate". The procedure mentioned that PQR should be done for API and intermediate manufactured in calendar from January to December. And it should be completed within three months from the date of completion of year. The QA Head was in charge of approving of PQR reports.

APQR of Piperaquine Phosphate

2018 APQR of Piperaquine Phosphate (PPQ) (PU4) were reviewed. There have been no WHO grade Piperaquine Phosphate (PU4) batches manufactured in year 2018.

2017 APPQ of Piperaquine Phosphate (PU4) was reviewed. There have been no WHO grade batches of Piperaquine Phosphate (PU4) manufactured in year 2017 as the API was not qualified by WHO. There were several OOS results related to the test of stability study samples. They were invalid and concluded they were caused by lab errors.

APQR of Amodiaquine hydrochloride

There were two manufacturing processes Q5 and Q6 for Amodiaquine hydrochloride API.

APQR of Amodiaquine hydrochloride (Q5) for year 2018 was reviewed. No OOT and OOS was recorded. One market complaint was received and investigated whereas there was no return and recall reported. The CPPs and in-process controls were reviewed. The stability study data were also reviewed. There was no OOS observed for stability samples. There were no reprocessing/reworking/ destruction batches in 2018.

APQR of Amodiaquine hydrochloride (Q6) for year 2018 for a foreign market was reviewed. No OOT and OOS was recorded. One market complaint was received and investigated whereas there was no return and recall reported. The CPPs and in-process controls were reviewed. There were no reprocessing/reworking/ destruction batches in 2018. The stability study data was also reviewed. There were two OOSs observed for stability samples.

The above mention APQRs were concluded that the process was manufactured consistently and met specifications and quality attributes of final products. Based on the assessments it was recommended to revalidate of the process due to changes in manufacturing equipment and review of cleaning validation study. Deficiencies noted in PQRs and listed in the full inspection report have been addressed in the CAPAs at a satisfactory level.

Quality Risk Management

A quality risk management procedure and risk assessment register were available and reviewed. The quality risk management report for amodiaquine HCL manufacturing was reviewed. Non-compliances observed during the inspection regarding risk management was listed in the full report. They were addressed by the manufacturer to a satisfactory level.

Deviation

Handling of deviation followed a written SOP. Deviation was classified into major or other. A deviation found in the control samples of Amodiaquine HCL was checked. Non-compliances observed during the inspection that was listed in the full report regarding deviation management were addressed by the manufacturer to a satisfactory level.

Internal audits (self-inspection)

The internal quality audits (self-inspection) procedures" Self-inspection – Active Pharmaceutical Ingredients and Intermediates" and "Corporate internal audit" were in place.

It was noted that self-inspections were conducted once every six months, in addition CQA conducts audits once every six months. The internal audit schedule for 2018 was reviewed and noted that planned audits were completed together with their compliance report. Similarly, the site audit scheduled for 2019 and the corporate annual audit schedule was also available and reviewed with no objectional findings.

Quality Management Review (QMR)

An SOP for management quality review was checked. Meeting minutes recorded in July 2019 was reviewed and found acceptable.

2. Personnel

Personnel qualifications

There were approximately 400 full time staff employed by the company at the time of inspection. The procedure "Personnel Responsibilities" was in place to define the responsibilities and described the job of personnel engaged in the manufacturing, processing, packing, testing or holding of APIs and Intermediates.

Job descriptions defining duties and responsibilities of key personnel were available. The following job descriptions were verified and found acceptable.

- Head of Quality Assurance
- Head of Quality Control
- Head of Production

Personnel hygiene

Personnel were required to wear protective clothing suitable for the type and stage of manufacturing. Smoking, drinking, eating and storage of food were not permitted in manufacturing areas. Any person shown to have an apparent illness or open lesions were rejected to engage in activities that could result in compromising the quality of APIs.

3. Buildings and facilities

WHO grades of Amodiaquine hydrochloride and Piperaquine phosphate APIs were manufactured at the following production blocks. All blocks were visited during the inspection.

- Plant 1: Micronization of APIs
- Plant 3: intermediate for Piperaquine phosphate
- Plant 5: Piperaquine phosphate & Amodiaquine hydrochloride
- PPA06: Drying of intermediates

The inspected production blocks and the production equipment were not dedicated. The last production steps i.e. drying, milling, sifting and packaging were carried out in class D. The risk of cross-contamination was controlled by means of a campaign-based manufacturing arrangement.

Non-compliances observed during the inspection that was listed in the full report regarding the facilities of PPA06 were addressed by the manufacturer to a satisfactory level.

HVAC system

A dedicated HVAC system provided filtered air to Grade D clean area of Plant 5 for final purification, crystallization, drying and packaging of APIs. HEPA filters were installed in class D clean rooms.

HVAC was managed according to the SOP “Performance and verification of air handling unit (AHU)”. The test of air velocity, HEPA filter integrity, particle count and temperature/humidity, as well as air flow pattern and recovery test were required to be performed at specified time interval. The qualification of a new production area was checked with no objectional findings.

Water system

The Demineralized water (DM) system reviewed was equipped with one generation system and three distribution loops. The sampling and testing of the DM water described in the SOP “Sampling schedule and procedure for water” and the SOP “Water quality monitoring” were reviewed with no objectional findings.

4. Process equipment

The workshop and equipment for manufacturing Piperaquine phosphate & Amodiaquine hydrochloride was not dedicated. Equipment used for manufacture of the APIs was of appropriate design and adequate size for its intended use. Labels attached to the equipment indicated equipment identification numbers, qualification status and due date were checked and discussed during the inspection.

5. Documentation and records

The documentation system was generally well established. A table with full revision history was included in each procedure. GMP related documents were prepared, reviewed, approved and distributed according to written procedures. A master list of SOPs was available.

Batch manufacturing records and batch testing records reviewed during the inspection were acceptable in general.

6. Materials management

General controls
A computerized system SCM (Supply Chain Management) was used in material management for the receipt and tracking of inventory.

Receipt and quarantine
Materials were required to be checked on receipt, including for damage and verification that the supplier was approved. They were then placed in quarantine and labelled before completion of sampling, testing and release.

Supplier management
Vendor audit was managed according to a corporate SOP. Key starting materials were required to be re-audit as specified in the SOP. The vendor audit annual schedule for 2019 and 2018 were checked and found acceptable.

7. Production and in-process controls

Production operations
Production in Plant 5 was in operation at the time of inspection. The BMRs, equipment status, equipment cleaning and line clearance in the intermediate staging room of Amodiaquine crude were inspected.

A product code list of Piperaquine Phosphate was available and reviewed. Different product codes for Piperaquine Phosphate was issued as per different manufacturing process and batch sizes.

In-process sampling and controls
In-process sampling was performed at defined and documented stages during processing. In-process samples were tested at the QC laboratory.

Blending batches of intermediates or APIs
Blending was not performed for the WHO grade of the APIs as stated by the company.

8. Packaging and identification labelling of APIs and intermediates

Packaging of Amodiaquine HCL API was carried out in Class D clean room. The packaging and labelling were not in operation at the time of the inspection.

9. Storage and distribution

Warehousing procedures
Finished APIs were stored in a designated warehouse and held until released by the Authorized Person. Storage condition was monitored and recorded.

Batch release
SOPs for batch release and for inspection of good for dispatch (API/intermediate) were available and reviewed. The release of an Amodiaquine HCL batch produced in 2019 and the BMR were checked. The observation made during the inspection that was listed in the full report regarding API product batch release were addressed by the manufacturer to a satisfactory level.

Distribution procedures
APIs were released for distribution following release by the Quality department.
API product return were checked in the computerized system during the inspection. The investigation was spot checked. Some observation regarding the CAPAs was made. They were addressed by the manufacturer to a satisfactory level.

10. Laboratory controls

The QC laboratories were responsible for physical, chemical and/or microbiological testing of starting materials, packaging materials, intermediates, finish APIs, environmental monitoring samples and purified water samples.

During the inspection, sample receiving, and distribution procedures, sample register and records were review and discussed.

The physical/chemical QC laboratory was equipped with HPLCs, GCs, UV, IR and other analytical instruments. The HLPCs and GCs were networked with software. UV and IR were stand-alone instrument with appropriate audit trails. The analytical data backup management checked was acceptable. Usage logs were available for instruments. Data management checked during the inspection was acceptable with no data integrity issues noted. Preventative maintenance procedure of analytical instruments was described in an SOP. The preventive maintenance plan of analytical instruments in 2019 was briefly reviewed and found acceptable.

Testing of intermediates and APIs

The following documents and records of API testing were reviewed.

- Analytical procedures and specification for Piperaquine phosphate
- Analytical procedures and specification for Amodiaquine hydrochloride USP.
- Analytical records of a batch of Amodiaquine hydrochloride API

Out of Specification (OOS) and Out of Trend (OOT) results

SOPs for management of OOS and OOT were reviewed. The logbooks of OOS and OOT were available, including those for finish API, raw material, intermediate and stability. Trending for handling of OOS/OOT results was required to be reviewed as per the SOP.

The OOS/OOT in 2017, 2018 and 2019 recorded regarding the WHO grade of APIs and their investigation were reviewed and discussed. Non-compliances observed during the inspection that was listed in the full report regarding the OOS management were addressed by the manufacturer to a satisfactory level.

Stability monitoring of APIs

Stability studies was performed according to an SOP. At least one batch of API manufactured during the year was required to be placed for ongoing stability study. The stability study chambers were inspected. The chamber monitoring record reviewed was acceptable.

Reserve/retention samples

The procedure for reserve samples management was reviewed. Reserve samples were stored in a designated temperature-controlled room (below 25°C). Samples of each batch of API manufactured were kept and stored in a container system that were comprised of the same materials as used for packaging of the finish API. A logbook was in place. The reserve samples were required to be retained for one year after the expiry date or for three years after distribution of the batch, whichever is the longer.

Microbiology laboratory

There was a dedicated area for the microbiology laboratory in the QC area. All microbiological tests of APIs, process water, purified water and environmental monitoring of microorganisms were performed by the laboratory which consisted of cleanroom and airlocks, unclassified area, microbiological section room, office (the interconnecting area between rooms), autoclave room and washing area room.

Media preparation and growth promotion tests were described in the SOP "Procedure for Media Management". Raw data of a batch of microbiological tests of amodiaquine hydrochloride was verified. The required tests and verifications were performed, and all results fulfilled the acceptance criteria (media preparation, sterilization of media and glass, growth promotion test, enumeration of microorganisms).

The last qualifications of LAF and Incubator performed in 2019 were reviewed and found acceptable.

Non-compliances observed during the inspection that was listed in the full report regarding the inadequate facility and area segregation of microbiological laboratory were under implementation by the manufacturer and required to be followed in next inspection.

11. Validation

A validation master plan (VMP) approved by Head of QA was available. The VMP for 2019 and qualification documents of a new centrifuge including DQ, IQ, OQ and PQ were reviewed and acceptable.

Process Validation

Process validation for Amodiaquine hydrochloride and Piperaquine Phosphate were carried out in 2012. The approach based on continuous process verification was used as an alternative to traditional process validation. The latest report on continuous process verification for Amodiaquine hydrochloride in 2019 was checked. Some deficiencies were observed. They have been addressed in CAPAs by the manufacturer to a satisfactory level.

Cleaning validation

Cleaning validation followed the SOP "Cleaning Validation for Active pharmaceutical ingredients and Intermediates". The last cleaning validation was carried out in 2012. It was noted that in 2012, three APIs including Amodiaquine Hydrochloride and Piperaquine Phosphate produced in Plant 5 were identified for the cleaning validation study. In 2014, when an additional new active substance was introduced, the limits were recalculated for four APIs.

An equipment cleaning validation report for Amodiaquine Hydrochloride was reviewed. All results fulfilled the acceptance criteria.

The processes of equipment cleaning were described in SOPs. All equipment was cleaned manually. Detergent was not used. The time interval between the end of production and the commencement of the cleaning procedure was specified. The dirty and clean equipment holding time for the equipment in Plant 05 was established based on study.

Some deficiencies concerning cleaning of equipment and cleaning validation were observed. They have been addressed in CAPAs by the manufacturer to a satisfactory level.

Analytical method validation

SOPs for analytical method validation and analytical method transfer were available and reviewed. All analytical method validations for WHO APIs were done by Ipca's R&D department located outside of Indore. Indore site conducted method transfer from R&D.

The analytical method validation for analysis of cleaning samples for WHO APIs were done by Indore site. Analytical method validation protocol for analysis of cleaning samples of amodiaquine hydrochloride and piperaquine phosphate was reviewed respectively. Some observations regarding analytical method validation for analysis of cleaning samples were noted. They have been addressed in CAPAs by the manufacturer to a satisfactory level.

Computerised system validation

The URS, IQ, OQ and PQ for laboratory information management system was briefly reviewed. The LIMS software was used in QC laboratory according to URS. This was not check in detail in this inspection.

12. Change control

Change control were managed according to a SOP for change control for API and intermediate. Several change controls related to equipment and analytical method validation were reviewed during the inspection. Non-compliances observed during the inspection that was listed in the full report regarding change control were addressed by the manufacturer to a satisfactory level.

13. Rejection and re-use of materials

Reprocess and reworking were performed according to a SOP. the company stated that no reworking has been applied for the PQed APIs since the last WHO inspection.

Solvent was recovered from various steps and used in the corresponding steps. An SOP for movement of fresh and distilled solvents and solvents recovery in plant 5 were reviewed. Some observations noted during the inspection have been addressed in CAPAs by the manufacturer to a satisfactory level.

14. Complaints and recalls

Complaints were managed according to a SOP. The procedure detailed the receipt and logging of complaints, investigation, timeline and CAPA. The complaints were logged in a logbook sorted by the product. The investigation of a product complaint in 2018 was reviewed with no objectional findings.

Recalls was managed according to a SOP. Recall procedure simulation was described in the SOP. Simulation was required to be performed once in two years. The most recent "mock recall" was performed in 2019. The company stated that there has been no product recall of Piperaquine phosphate and Amodiaquine hydrochloride API products in the last three years.

15. Contract manufacturers (including laboratories)

There was no contract manufacturing and testing conducted for WHO APIs.

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 Limited(Indore),*** located at ***89 A-B/90/91 & 78/79/80 across the public road (Opp.89/90), Industrial Estate Polo-ground Indore-452003, Madhya Pradesh, India*** for the manufacturing of the API, **Amodiaquine HCl (APIMF030) and Piperaquine Phosphate (APIMF227)** 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 2 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 GMP for APIs or WHO TRS No. 957, Annex 2***
   http://apps.who.int/medicinedocs/documents/s20119en/s20119en.pdf

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 GMP*** or ***WHO TRS No. 986, Annex 2***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

3. WHO good manufacturing practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-sixth Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2.
   Short name: WHO TRS No. 970, Annex 2
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/

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
   http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

5. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8. ***Short name: WHO HVAC Guidelines*** *or* ***WHO TRS No. 1010, Annex 8***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_1010/en/

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

7. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1.
   Short name: WHO TRS No. 957, Annex 1
   http://www.who.int/medicines/publications/44threport/en/

8. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2.
   Short name: WHO TRS No. 957, Annex 2
   http://www.who.int/medicines/publications/44threport/en/

9. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 6.
   Short name: WHO TRS No. 961, Annex 6
   http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7.
    Short name: WHO TRS No. 961, Annex 7
    http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

11. Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9. ***Short name: WHO TRS No. 961, Annex 9***
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

12. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-first Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. ***Short name: WHO TRS No. 943, Annex 3***
http://whqlibdoc.who.int/trs/WHO_TRS_943_eng.pdf?ua=1

13. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2.
Short name: WHO TRS No. 961, Annex 2
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

14. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2. ***Short name: WHO TRS No. 981, Annex 2***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/
15. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3. ***Short name: WHO TRS No. 981, Annex 3***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/
16. WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14. ***Short name: WHO TRS No. 961, Annex 14***
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

17. WHO Guidelines on good manufacturing practices: validation, Appendix 7: non-sterile process validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 3. ***Short name: WHO TRS No. 992, Annex 3***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

18. WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4. ***Short name: WHO TRS No. 992, Annex 4***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

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

20. WHO Recommendations for quality requirements when plant – derived artemisin is used as a starting material in the production of antimalarial active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 6
Short name: WHO TRS No. 992, Annex 6
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

21. Guidance on good data and record management practices. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5.
Short name: WHO GDRMP guidance or WHO TRS No. 996, Annex 5
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf

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

23. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 10.
Short name: WHO TRS No. 1010, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf