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

Part 1	**General information**
Manufacturers details	
Name of manufacturer	Ipca Laboratories Ltd. Athal
Corporate address of manufacturer	Ipca Laboratories Limited Registered Office : 48, Kandivli Industrial Estate, Kandivli (West), Mumbai 400067 (Maharashtra), India Tel : +91 (22) 6647 4444
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Ipca Laboratories Limited Plot No. 255/1, Village-Athal, Silvassa - 396230, Union Territory of Dadra and Nagar Haveli and Daman and Diu, India Tel : +91 260 6164200/246/355 20°15'27.00"N, 72°57'55.6"E
Unit / block / workshop number	N/A
Inspection details	
Dates of inspection	27-29 June 2023
Type of inspection	Routine GMP Inspection The inspection covered all areas of GMP and focused on the investigation of OOS test results in Artesunate/Amodiaquine 25/67.5mg stability studies
Introduction	
Brief description of the manufacturing activities	The site is authorized to manufacture tablets and hard gelatin capsules for human use. No steroids, cytotoxic, beta lactam and hormonal products are manufactured on site
General information about the company and site	Ipca Laboratories were established in 1949. The company manufactures and markets a wide range of pharmaceutical formulations and APIs and has several facilities in India and abroad. The production facilities at Athal were established in 1995 and the built-up area covers 42208m^2. Whereas total Plot area is 104000m^2
History	The most recent on-site WHO inspection was carried out in April 2015. A desk assessment was conducted in August 2019

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Documents reviewed included but were not limited to: • Quality Manual – management review meetings • Organization Chart • Job descriptions for key personnel • Personnel training and hygiene • Product Quality Review • Quality Risk Management • Responsibilities of the quality unit and production • Complaints and Recalls • Deviation handling and CAPA • Change control • OOS and OOT investigations • Material release • Self-inspection and vendor qualification • Validation and qualification • Equipment calibration • Data integrity • Sampling and testing of materials • Batch processing records • Materials management system • Analytical methods – stability • HVAC system • PW/ systems Areas visited: • Starting materials, packaging materials and FPP warehouses • Sampling and dispensing areas • Manufacturing operations for FPP • QC laboratories (Analytical)
Restrictions	N/A
Out of scope	Products not submitted to Prequalification were excluded from the scope of this inspection
WHO products covered by the inspection	Artemether/Lumefantrine Tablet, Dispersible 20mg/120mg Artemether/Lumefantrine Tablet 20mg/120mg Artemether/Lumefantrine Tablet 80mg/480mg Amodiaquine (hydrochloride)/Artesunate Tablet 67.5mg/25mg Amodiaquine (hydrochloride)/Artesunate Tablet 135mg/50mg Amodiaquine (hydrochloride)/Artesunate Tablet 270mg/100mg Pyrimethamine/Sulfadoxine + Amodiaquine (hydrochloride) Tablet, Dispersible 12.5mg/250mg + 76.5mg (pending) Pyrimethamine/Sulfadoxine + Amodiaquine (hydrochloride) Tablet, Dispersible 25mg/500mg + 153mg (pending)

Con formato: Francés (Bélgica)

	Pyrimethamine/Sulfadoxine Tablet, Dispersible 12.50mg/250mg (pending) Pyrimethamine/Sulfadoxine Tablet, Dispersible 25mg/500mg (pending) DI011 Zinc (sulfate) Tablet, Dispersible 20mg HA744 Sulfamethoxazole/Trimethoprim Tablet 400mg/80mg HA745 Sulfamethoxazole/Trimethoprim Tablet 800mg/160mg
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 Packaging 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 air flow
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 principles of the QMS were adequately described in the Quality Manual including but not limited to the Quality Policy and objectives, responsibilities of senior management, management of changes and non-conformances, handling of market complaints and recalls. A procedure for the preparation of the QM was in place. The GMP guidelines were typically followed. Production and quality assurance departments were independently managed, and their operations were described in documented procedures. Job descriptions outlined managerial responsibilities. Products and operations were tracked and supervised. There were procedures in place for the periodic assessment of processes and operations and release of products.

Management review meetings

Management review meetings were organized at corporate level and held in accordance with a written procedure. Corporate QA was assigned as the meeting coordinator and was responsible for preparing the agenda for the meetings which were held quarterly. Senior representatives from each site provided a presentation on set topics of interest. Further to these meetings there were on-site technical meetings that were held every two weeks focusing on site specific issues.

Product Quality Review

The corporate procedure on conducting PQRs was reviewed. The corporate SOP allowed for some flexibility on the compilation of the reports to be done either following the calendar year (i.e., January to December) or on a rolling period of 12 months. The IPCA Athal site was performing PQRs on a rolling basis, though this decision was not documented. The 2023 plan was presented. PQRs had to be completed within 3 months from the defined review period. Statistical tools were used to evaluate critical process parameters and product quality attributes.

The following PQRs were reviewed:

- Artesunate/Amodiaquine 25/67.5mg tab (Oct. 2021-Sep. 2022)
- Cotrimol tablets 800/160mg (Apr. 2022 – Mar. 2023). Only 3 registration batches were manufactured during the review period.
- Cotrimol tablets 400/80mg (Apr. 2022 – Mar. 2023). Only 3 registration batches were manufactured during the review period.
- Pediatric Zinc Sulphate tablet 20mg Ph.Int. (Oct 2021- Sep. 2022). Only 3 registration batches were manufactured during the review period.

Change Control

There was a system in place for managing changes which defined the process of initiating, registering, approving, or rejecting, monitoring, and implementing changes, as well as defining roles and responsibilities. Changes were registered and monitored in TrackWise. The following changes were spot checked:

- Introduction of an additional supplier for Zinc Sulphate
- Zinc Sulphate validation batches to be carried out due to the addition of a new Zinc Sulphate supplier.

DeviationsThe procedure on handling deviations was reviewed. Deviations had to be registered in TrackWise within 24 hours of identifying an unexpected departure from standards, specifications, or established procedures. Recurrence was checked and registered. QA was responsible for assigning criticality to a deviation (major or minor). Root cause investigations had to be carried out and tools for carrying out such investigations were defined. Several examples of deviations' handling were reviewed

All the non-compliances relating to PQS elements were addressed by the manufacturer, to a satisfactory level.

2. Good manufacturing practices for pharmaceutical products

Manufacturing processes were generally clearly defined and systematically reviewed. Qualifications/ validations, calibrations and maintenance were performed according to prepared protocols and followed the relevant established procedures. Necessary resources including qualified and trained personnel, adequate premises, suitable equipment and services, appropriate materials, approved procedures, and instructions were provided for the current operational level of manufacturing and testing. There were processes in place for identifying and registering deviations, for monitoring the application and tracking the implementation of corrective and preventive measures. Manufacturing steps were recorded in batch manufacturing and packaging records. BMRs and BPRs were made available during the tour of the facilities.

All the non-compliances observed during the inspection that were listed in the full report were addressed by the manufacturer, to a satisfactory level.

3. Sanitation and hygiene

Premises and equipment were maintained at a satisfactory level of cleanliness at the time of inspection. There was appropriate gowning in all areas for staff and visitors, including pictorials and hand washing and sanitization before entry to production areas. The company had procedures in place for personal hygiene and behavior as well as for sanitation, disinfection. Areas were cleaned frequently in

accordance with an approved written program and SOPs. Microbial monitoring was regularly performed

All the non-compliances observed during the inspection that were listed in the full report were addressed by the manufacturer, to a satisfactory level.

4. Qualification and validation

The VMP was established based on a corporate SOP. The 2023 VMP was reviewed. The document described the overall philosophy and strategy of the company towards validation/qualification including but not limited to, the scope, plan, activities, frequency, and responsibilities. The plan was prepared by the QA department and reviewed by all department heads. The document was approved by the site head and the QA head.

Further to the VMP a procedure was in place providing details on equipment, system and facility (re)qualification. The 2023 Periodic Verification Plan was presented.

Blister Packing Machine

The original PQ protocol of the blister packing machine was reviewed. The initial qualification had taken place in 2015. The latest requalification was conducted according to a written protocol, in December 2021. The Periodic Verification Report was reviewed in detail.

Dispensary HVAC and Dispensing Booth

The procedure on the performance qualification and periodic verification of HVAC Systems and devices/equipment provided with HEPA filters was reviewed. The periodic verification report of the HVAC system supplying air to the Dispensing-I area was presented. Air-velocity/air-changes, filter integrity, temperature/relative humidity, non-viable particle count, microbial monitoring (settle plate, active air-sample, contact plate), recovery test and smoke test were included among the tests.

The latest periodic verification of the dispensing booth was presented. Calibration certificates for standard equipment (i.e., anemometer, aerosol photometer, particle counter, magnehelic gages) were available. Raw data for microbial monitoring and non-viable particles were checked in detail.

Process validation

Process validation was carried out according to a corporate SOP. The process validation of Zinc Sulfate DT 20mg was reviewed. The validation was triggered because an additional API supplier was introduced. Three consecutive batches were manufactured during January-February 2022. The manufacturing process consisted of sifting starting materials, dry mixing, further sifting, blending, lubrication and compression. Process parameters and critical quality attributes were identified and monitored during manufacturing. Raw data for analytical testing was made available.

All the non-compliances relating to validation/qualification activities that were listed in the full report were addressed by the manufacturer, to a satisfactory level.

5. Complaints

The list of complaints for 2022 and the relevant procedure were reviewed. QA at corporate level was responsible for handling complaints with the assistance of the site. Complaints were categorized as critical, major, or minor. Investigations for serious complaints had to be concluded within 7 days. Eight complaints were listed for 2022-2023 (until the time of inspection), while only three were registered in 2021 and zero in 2020. Several complaints from 2022-2023 were reviewed, along with relevant root cause investigations and CAPA.

All the non-compliances observed during the inspection that were listed in the full report were addressed by the manufacturer, to a satisfactory level.

6. Product recalls

There were two procedures in place to recall products from the domestic market and from export markets respectively. The SOPs provided appropriate instructions for recalling products from the market in a timely manner. The responsibilities for recalling were assigned to the site and corporate QA heads, and the marketing and distribution head. Recalls were classified into 3 levels.

An example of a recall taking place in 2022 was reviewed

A mock recall was performed annually in case no recall was performed during the previous year. The 2021 mock recall was reviewed.

All the non-compliances observed during the inspection that were listed in the full report were addressed by the manufacturer, to a satisfactory level.

7. Contract production, analysis, and other activities

Production operations were not contracted out. Certain tests were carried out by approved laboratories which were monitored and evaluated for performance, (re)qualified and audited.
Contracts with laboratories were handled according to a corporate SOP.

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

Supplier evaluation and qualification was conducted according to two established corporate procedures. Initially a paper assessment and a sample evaluation were carried out. In addition, the vendor was periodically assessed in terms of quality, delivery (punctuality, quantity), pricing. Audits of suppliers were managed according to a written procedure and were based on risk. Criteria for qualifying auditors were established and a list of qualified auditors was presented.

Examples of suppliers' qualifications, audit reports, periodic evaluations and technical agreements were reviewed.

All the non-compliances observed during the inspection that were listed in the full report were addressed by the manufacturer, to a satisfactory level.

9. Personnel

There were approximately 1200 staff working on site. In general, personnel had the necessary qualification and practical experience. Personnel interviewed during the inspection had sufficient knowledge of GMP standards. Responsibilities of staff and their duties were documented in written job descriptions according to an established SOPs. Examples of job descriptions of key personnel and their qualifications were reviewed.

10. Training

The training procedure was reviewed. Training was divided into induction training, cGMP, on the job training and external training. Trainings were evaluated with questionnaires and passing grade criteria were set. The human resources department prepared the annual training plan. The 2022 training plan was presented. Spot-checks on new and revised SOP trainings and training records were made.

Each SOP included a section that identified the personnel that needed to undergo training. Training was provided before the new SOPs became effective. New or revised corporate SOPs had to be

implemented within 30 days from the time they were uploaded in the EDMS system. During that period key personnel from each site had to be trained on the SOP and then train personnel on-site.

All the non-compliances observed during the inspection that were listed in the full report were addressed by the manufacturer, to a satisfactory level.

11. Personal hygiene

Procedures were in place for the conduct of medical examinations for all personnel upon recruitment, and thereafter annually. Personnel were encouraged to report any illness that might affect the quality of the product to their supervisors. Personnel hygiene measures such as handwashing, routine hand sanitisation and appropriate gowning were observed in core manufacturing areas. There was a procedure in place for personnel gowning

12. Premises

Layouts of the facilities were made available. In general, premises were constructed, designed, and maintained to suit the operations to be carried out and prevent the risk of contamination of materials and products. At large, the design of premises was such as to minimize the risk of errors and permit effective cleaning, disinfection, and maintenance. Changing rooms were flushed with filtered air and in most cases appropriate differential pressures were established between rooms for containment purposes. Clean areas were maintained to an appropriate standard of cleanliness and supplied with air that has passed through HEPA filters. Temperature and relative humidity were monitored and controlled.

Storage areas were of sufficient capacity. Segregation was provided for the storage of rejected, recalled, or returned materials or products. Spot checks on rodent traps, insecticutors and their relevant maintenance cards were made.

All the non-compliances observed during the inspection that were listed in the full report were addressed by the manufacturer, to a satisfactory level.

13. Equipment

Production equipment was of good standard and appeared to be well maintained. Spot-checks on production balances and differential pressure gauges indicated that equipment and devices were timely calibrated. The workflow in the facility was appropriately designed, and the equipment appeared to be installed to facilitate production and reduce the risk of contamination and mix ups. All production equipment reviewed was identified as to its content or purpose, with cleanliness status identified by appropriate labels. Spot-checks on equipment maintenance logbooks and equipment use logbooks were made.

All the non-compliances observed during the inspection that were listed in the full report were addressed by the manufacturer, to a satisfactory level.

14. Materials

Written procedures for the receipt, identification, quarantine, storage, handling, sampling, approval, or rejection of materials were checked. A Supply Chain Management (SCM) system was used for the management of materials. Starting materials were purchased from approved suppliers. Material receipt operations were inspected in detail as well as management of stock. Incoming starting materials were

quarantined after receipt until they were released for use. Temperature and relative humidity conditions were monitored.

All the non-compliances observed during the inspection that were listed in the full report were addressed by the manufacturer, to a satisfactory level.

15. Documentation

In general, documents were designed, prepared, reviewed, and distributed with care. They were approved, signed, and dated by the appropriate responsible persons. Documents were regularly reviewed and kept up to date. Records were made or completed when any action was taken. The documentation reviewed during the inspection indicated that there were two types of SOPs (corporate and site specific). An EDMS was in place which allowed for the timely revision and monitoring of SOPs. In general, Corporate SOPs were not implemented until Key personnel from each Ipca site was appropriately trained.

All the non-compliances observed during the inspection that were listed in the full report were addressed by the manufacturer, to a satisfactory level.

16. Good practices in production

In general production operations followed defined procedures and records of activities were maintained. Checks on yields and reconciliation of quantities were carried out. Before processing operations were started, steps were taken to ensure that the work area and equipment were clean and free from any starting materials, products, product residues, labels or documents not required for the current operation. Environmental monitoring was conducted. Weighing and measuring devices were of suitable accuracy for the intended use. Calibration procedures and records for scales were presented. Dispensed material followed the established material flow. Necessary in-process controls were carried out and recorded. Similarly, before packaging operations began, steps were taken to ensure that the work area, packaging line, printing machine and other equipment were clean and free from any products, materials or documents used previously.

All the non-compliances observed during the inspection that were listed in the full report were addressed by the manufacturer, to a satisfactory level.

17. Good practices in quality control

Quality Control (QC) operations were independent of production. The QC laboratories were appropriately designed and equipped with the necessary physicochemical and microbiological testing equipment. The laboratories comprised of different sections such as chemical, instrumental, packaging material analysis, raw material analysis and microbiological. Calibration/qualification procedures and plans for equipment were in place. Equipment was uniquely identified and labelled. Examples of records for the daily verification and monthly calibration of the laboratory balances were checked.

Retention samples of finished product were kept one year after the expiry date in a separate area, according to a written procedure. An annual visual check was performed for physical integrity.

Stability studies were designed and carried out in accordance with a procedure. One batch per product per year was placed in on-going stability studies.

There was a procedure in place for performing investigations on OOS test results. Investigations were carried out in 3 phases:

- Phase I: preliminary investigation to allow elimination of obvious errors
- Phase II: more in-depth investigation under QA oversight which consisted of a more expanded manufacturing and laboratory investigation.
- Phase III: a review of all manufacturing and laboratory records and investigations and identification of potential root cause.

In case the OOS results were confirmed, a non-conformance report would be registered according to the procedure for conducting stability studies.

OOS investigations in relation to Artesunate/Amodiaquine 25/67.5mg tab were reviewed in detail. More specifically raw data from Phase I, Phase II and Phase III investigations were presented. Additional investigations were conducted and were adequately documented. The non-conformance report was made available, as well as documentation detailing corporate decisions.

All the non-compliances observed during the inspection that were listed in the full report were addressed by the manufacturer, to a satisfactory level.

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 Athal*** located at ***Plot No. 255/1, Village-Athal, Silvassa - 396230, Union Territory of Dadra and Nagar Haveli and Daman and Diu, 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://digicollections.net/medicinedocs/documents/s21467en/s21467en.pdf

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***
   untitled (digicollections.net)

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
9789240020900-eng.pdf (who.int)

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://digicollections.net/medicinedocs/documents/s21440en/s21440en.pdf

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 TRS No. 1010, Annex 8**
https://digicollections.net/medicinedocs/documents/s23455en/s23455en.pdf

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
https://digicollections.net/medicinedocs/documents/s20108en/s20108en.pdf

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. 961, 957), Annex 1
https://digicollections.net/medicinedocs/documents/s18681en/s18681en.pdf

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 3.
Short name: WHO TRS No. 957, Annex 3
https://digicollections.net/medicinedocs/documents/s22358en/s22358en.pdf

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
https://digicollections.net/medicinedocs/documents/s19959en/s19959en.pdf

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
https://digicollections.net/medicinedocs/documents/s18677en/s18677en.pdf

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**
https://digicollections.net/medicinedocs/documents/s18683en/s18683en.pdf

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***
https://digicollections.net/medicinedocs/#d/s21438en

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
https://digicollections.net/medicinedocs/documents/s18682en/s18682en.pdf

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
https://digicollections.net/medicinedocs/#d/s20177en/

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
https://digicollections.net/medicinedocs/#d/s20175en/

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. 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://digicollections.net/medicinedocs/documents/s23697en/s23697en.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***
Essential Medicines and Health Products Information Portal (digicollections.net)

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
https://www.who.int/publications/m/item/who-recommendations-for-quality-requirements-when-plant-derived-artemisinin-is-used-as-a-starting-material-in-the-production-of-antimalarial-active-pharmaceutical-ingredients---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***
9789240020900-eng.pdf (who.int)

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
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

24. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditionning 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://digicollections.net/medicinedocs/documents/s23699en/s23699en.pdf

25. 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**

9789240020900-eng.pdf (who.int)

26. 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**
9789240001824-eng.pdf (who.int)

27. 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-detail/978-92-4-000182-4

28. 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-detail/978-92-4-000182-4