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

Part 1	**General information**
Manufacturers details	
Name of manufacturer	Maphar Laboratories
Corporate address of manufacturer	Km 10, Route Côtière 111, Quartier Industriel Zenata – Aïn Sebaâ, Casablanca, Marocco
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Same as above
Unit / block / workshop number	OSD Block
Inspection details	
Dates of inspection	19 – 22 November 2019
Type of inspection	Routine GMP inspection
Introduction	
Brief description of the manufacturing activities	Production and quality control of finished pharmaceutical products including OSDs, semisolids and liquids.
General information about the company and site	The manufacturing site of Maphar is located at Zenata industrial estate, Aïn Sebaâ, Casablanca, Marocco. Maphar Laboratories became a joint venture between Eurapharma and Sanofi in June 2017. According to the opening meeting presentation and review of the Site Master File Maphar has: • one manufacturing site based in Zenata industrial estate of Casablanca • a distribution centre located in Ain Sebaa, Casablanca. The WHO finished product Artesunate/Amodiaquine tablets (ASAQ) is stored in this centre before being dispatch for onward distribution. The Zenata manufacturing site produces various dosage forms such as oral solid (tablets, capsules and granules), liquids and semisolids. The company stated that penicillin, cephalosporin and other high potent products were not manufactured on the site. From the presentation, it was also noted that Zenata employs 340 staff.

History	The last WHO Prequalification inspection of Maphar Laboratories, Zenata manufacturing site was conducted in November 2016. In addition, the site was inspected by Ministry of Health (MoH), Morocco in 2019. But no inspection from any PIC/S inspectorate were performed since 2016.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	• Quality management system • Production block and warehouses • QC laboratories • Water system • Changes made since last inspection • Validation and qualification/
Restrictions	None
Out of scope	The scope of the inspection was restricted to the following FPPs in the WHO PQ program.
WHO products covered by the inspection	MA056: Artesunate/Amodiaquine (as Hydrochloride) 25mg/67.5mg tablets MA057: Artesunate/Amodiaquine (as Hydrochloride) 50mg/135mg tablets MA058: Artesunate/Amodiaquine (as Hydrochloride) 100mg/270mg tablets
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
APS	Aseptic process simulation
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GMP	Good manufacturing practices
GPT	Growth promotion test
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IQ	Installation qualification
LAF	Laminar 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**

1. Pharmaceutical quality system

In general, a pharmaceutical quality system was implemented. The production and quality control operations were specified in written forms and GMP requirements were generally followed. Managerial responsibilities were specified in job-descriptions. Product and processes were monitored, and the results were considered in batch release and regular reviews of the quality of pharmaceutical products were conducted. Periodic management reviews were performed. The site uses several computer-based applications for management of change controls, deviations and CAPA, laboratory data management, document management, material management etc.

Quality Risk management

A quality risk management SOP and annual risk assessment plan were available and reviewed. Non-compliances observed during the inspection that was listed in the full report regarding quality risk management were addressed by the manufacturer to a satisfactory level.

Product quality review (PQR)

An PQR procedure was in place which described purpose and application of the procedure. Various elements of quality systems and products were reviewed on an annual basis and required to be completed within specified timeline as per the procedure.

The following APQR were reviewed during the inspection and found acceptable.

- The PQR for ASAQ (25/67.5 mg, 50/135 mg and100/270 mg) for 2018. All batches manufactured in 2018 were released. Deviation, OOS and change control were noted and reviewed. No complaint, return or recall was received. Stability results were within specifications. The shelf-life was recorded as 36 months. All the equipment, as well as the HVAC systems used for the production, were qualified at per due date.

- The PQR for ASAQ (25/67.5mg, 50/135mg and100/270mg) for 2017. The batches released were documented. Deviations, complaint, CAPAs, contract testing, quality agreement, change controls and OOT were noted and reviewed. No recall was initiated for any strength of ASAQ.

Batch release

An SOP for the release of finished products was reviewed. The SOP described the specific release process related to the products manufactured and controlled by Maphar. No deficiency was noted.

Change control

The following documents were reviewed:

- An SOP for change control. The current version of SOP was managed in an electronic quality management system and applicable for the entire Quality system.
- A change control report related to the modification of the quality system and documentation management. All actions were implemented. The change control had been closed at the time of inspection.

Deviation

The following documents were reviewed:

- An SOP for deviations handling.
- Report of a quality event (deviation) related to a stability chamber. The list of products was recorded. The investigation revealed that the electrical power shutdown caused a short-circuit on the equipment. In conclusion of the investigation, it was resolved that these incidental conditions would not have any significant impact on the analytical results of the concerned products. After repairing, the equipment was requalified, however failed again. At the time of inspection, the equipment was not in use and the products were moved to the backup stability chamber

2. Good manufacturing practices for pharmaceutical products

Good manufacturing practices were generally implemented and followed. Necessary human and physical resources were provided for the current operational level of FPP activity. Manufacturing processes were adequately defined and documented. Qualification and validation were performed according to company procedures.

The site organizational structure was considered adequate. In the manufacturing areas, the material and personnel flows were adequately separated. During the inspection, it was observed that personnel was dressed in adequate protective clothing as per the activities to be performed. The design and interior finishes of the workshops and QC laboratories were considered suitable.

3. Sanitation and hygiene

The company had an SOP as the basis for its approach to personal hygiene and sanitation relating to the production facilities. Areas were found clean and well maintained.

4. Qualification and validation

Validations and qualifications were performed according to the site policy and documented procedures. A validation master plan was available for inspection. CPP and CQA were required to be validated. For equipment and process validation the company had identified the qualification and validation work as required.

Process validation (PV)

Process validation was managed according to an SOP. Revalidation could be trigged by changes. If there was no change, the need of revalidation was based on APQR. This was specified in the SOP for PQR. PV planning and schedule for the PV to be performed in 2019 was available.

Process validation protocol/report of ASAQ 25mg/67.5mg performed in 2016 was reviewed. It was trigged by a change control due to Amodiaquine specification change of an API supplier. A new product code was introduced based on the change control.

Process validation for ASAQ 50mg/135mg was performed in 2013. The report was reviewed and discussed.

Equipment cleaning validation

For equipment cleaning validation, the following documents were reviewed:

- An SOP for cleaning validation of manufacturing equipment.
- A classification document of the products on the site. The classification of the APIs used for ASAQ were identified and documented.
- List of the products handled on a shared equipment Compactor granulator.
- Protocol for the cleaning validation of the Compactor granulator used for production ASAQ.
- Cleaning validation Report for the Compactor granulator used for production of ASAQ. Three batches of ASAQ 100/270 mg were used for the cleaning validation. The maximum "dirty holding time" was established before cleaning.
- Cleaning instruction for the cleaning of the Compactor granulator used for production of ASAQ. Different types of cleaning were described in the procedure.
- Validation report for the cleaning of the Compactor granulator after continuous manufacturing of batches of ASAQ.

Non-compliances observed during the inspection that was listed in the full report regarding cleaning validation and process validation were addressed by the manufacturer to a satisfactory level.

Computerized systems validation (CSV)

Computerized system validations were managed according to an SOP. Documents reviewed including upgrade of LIMS, QC lab computerized system validation, risk analysis and procedure on management of electronic data of HPLC were acceptable.

Water system

For production of purified water, the following documents were reviewed:

- Qualification report of installation and operation of the production and distribution of the purified water network.
- Initial performances qualification report of the water treatment system.
- A complete binder containing all the information on the welding of the distribution network.
- A PQ report of the purified water distribution network.
- A calibration and verification report of the temperature and conductivity gauges located at the return of the purified water loop.
- An SOP for the sampling of the purified water.
- Trends analysis report for the quality of the purified water for 2018.

No deficiencies were noted.

HVAC

The following documents reviewed:

- A plan of equipment and HVAC maintenance in 2019.
- Performance qualification of a HVAC system.

No deficiencies were noted.

5. Complaints

Complaints were managed according to an SOP. Complaints were classified into four levels. Class I is the highest according to criticality. A flow chart for handing complaints is available and documented. Compliant registers were available for review. No complaint on ASAQ was received in 2019.
In 2018 one complaint on ASAQ was received regarding label missing, box damage and box missing, and a CAPA was implemented. No comments were made.

6. Product recalls

Product recall was managed according to an SOP. The procedure covered products made as well as products distributed by Maphar. There were three classes of recall. If there is no recall during the year, a mock recall will be performed.

The recall of ASAQ is managed by Sanofi. There has been no recall of ASAQ tablets since the last inspection.

7. Contract production, analysis and other activities

A quality agreement between Maphar and Sanofi-Aventis Maroc was available for specified contract testing and manufacturing.

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

A self-inspection procedure described the objective, scope, reference document, definitions, procedure etc. was in place. Self-inspection was performed on the regular basis according to a pre-scheduled time table. A list of qualified auditors was available which consisted of QA auditors as well as experts from other departments. QA department participated in all the self-inspection audits. Observations were classified, and timeline were defined as for reporting and for CAPA.

9. Personnel

The manufacturer had defined and documented the organization and management structure. The responsibility, authority and interrelationship of the personnel was specified in the organization chart.

The company had an adequate number of personnel in manufacturing areas and laboratory. For responsible staffs, the duties were recorded in written job descriptions. Measures were taken to prevent unauthorized people from entering production, storage and QC areas. The Laboratory maintained current job descriptions for all personnel involved in tests and/or calibrations, validations and verifications. The laboratory also maintained records of all technical personnel, describing their qualifications, training and experience.

10. Training

An SOP for training and qualification of the personnel was reviewed. It included internal and external training. Training were evaluated by documented assessment. Training plane was done on annual basis and plane for 2019 and 2020 was set according to staff need.

11. Personal hygiene

During the inspection visit, it was noted that the people wore suitable garments and had a correct behavior in the manufacturing and testing areas. The gowning procedure was available in changing rooms and the gowning instructions depicted were complete.

12. Premises

Documented layouts of the facilities were available. Generally, premises were located, designed, constructed and maintained to suit the operations to be carried out.

Exposed surfaces were smooth, impervious and unbroken. Changing rooms were designed as airlocks and used to provide physical separation of the different stages of changing. Airlock doors were interlocked. Premises were cleaned and disinfected according to written procedures. Rest and refreshment rooms were separate from manufacturing and control areas.

Storage areas were of sufficient capacity. Receiving and dispatch bays protected materials and products from the weather. Segregation was provided for the storage of rejected, recalled, or returned materials or products.

Separate sampling areas were provided for sampling of APIs, excipients, primary and secondary packaging materials. APIs, excipients and primary materials were sampled under laminar airflow (LAF).

Dispensing for APIs/inactive materials and primary packaging materials was carried out in dispensing rooms under LAF. Dispensing was carried out by warehouse officer and checked by the production officer. Materials were dispensed in poly bags and stored in stainless steel containers / cages.

Environmental monitoring (EM) was performed according to written procedures, including plate settling count, air sampler count. Alert limit and action limits were set based on historical data.

The following documents were reviewed:

- An SOP related to the temperature and humidity mapping of the storage areas.
- A mapping report for the winter season of the storage area.
- A mapping report for the summer season of the storage area.
- An SOP for temperature and monitoring of a warehouse.
- Temperature and humidity mapping report for a warehouse performed during the summer season.
- Temperature and humidity mapping report for a warehouse performed during the winter season.

13. Equipment

Both dedicated and shared equipment were used for ASAQ manufacture. The following documents were reviewed and found acceptable.

- An SOP for the organization of the metrology.
- An SOP for the organization of the maintenance (preventive or curative) of the equipment and premises.
- Annual schedule for the preventive maintenance of the production equipment for 2019.
- A preventive maintenance report for a compactor.
- A preventive maintenance report for the tablet press machine.
- A preventive maintenance report for the blistering equipment.
- An SOP for design, usage, cleaning and maintenance of HVAC systems.

HVAC

The environmental conditions in the production areas were controlled by HVAC system bearing HEPA filters in manufacturing areas. In order to avoid cross-contamination the access in the manufacturing cubicle was controlled by airlock which was maintained in overpressure with respect to the cubicle and main corridor.

14. Materials

The APIs used for AQSQ tablets were supplied by approved suppliers. No batch of those APIs were rejected.

The following documents were reviewed and found acceptable.

- An SOP for the approval of a new material manufacturer.
- An audit report related to the manufacturer of Artesunate API.
- An audit report related to the manufacturer of Amodiaquine HCl API.

15. Documentation

An SOP for good documentation management was reviewed. Documents were designed, prepared, reviewed and distributed with care. Documents were approved, signed and dated by the appropriate responsible persons. Documents were regularly reviewed and kept up to date. All documents are saved in a computerised system.

The Master BMR and BMRs of a selected batch of ASAQ were reviewed. The BMRs were required to be kept on site over a specified period then transferred to archiving facility according to company procedure.

16. Good practices in production

At the time of inspection, the production line was in operation. The manufacturing and packaging operations observed in inspection were performed at an adequate level to meet the GMP requirements.

A procedure for material dispensing of campaign batch was available and reviewed. Punch and die usage log book was checked. Equipment log books were kept in place.

An SOP for reworking and reprocessing and an ASAQ batch deviation in tablet pressing process were reviewed. No deficiencies were noted.

For the use of nitrogen during production, the following documents were reviewed:

- Analytical method for the testing of Nitrogen.
- Analytical reports for the cylinders of Nitrogen used in 2019.

17. Good practices in quality control

Laboratory premises were separated from production areas. Laboratory had adequate space for the orderly placement of equipment and materials and to perform tests. Access to laboratory premises was restricted to authorized personnel.

Testing of FPPs
The sample receiving, and distribution were inspected. Log books were kept.

ASAQ primary reference standards were used for analysis, was purchased from EDQM and USP. Impurities standards were purchased from commercial sources.

The document "Preparation of certificate of analysis" was checked. CoA was prepared by QC supervisor, reviewed by QC manager and approved by QA manager.

Stability monitoring of FPPs
A range of stability chambers were available in R & D and QC lab. Stability monitoring program and samples were checked. Long term stability study for WHO grade of ASAQ was performed under the condition of 30ºC, RH 65% according to the procedure.

Reserve/retention samples
Retention samples were kept in a room maintained at 15 to 25ºC and RH was monitored but not controlled. Samples were packed in the same packaging system in which the FP packed for marketing. Samples were stored year after the expiry date assigned by the manufacturer to the batch.

OOS management
An OOS & OOT procedure was available and reviewed. The OOS and OOT for the year 2018 for ASAQ was reviewed. An OOS for single unknown impurity test was reviewed and the data integrity were checked. Non-compliances observed during the inspection that was listed in the full report regarding data management in QC laboratory were addressed by the manufacturer to a satisfactory level.

Microbiological laboratory
Microbiological laboratory premises were separated from chemical laboratory. Laboratory was separated by cross-bench at the entrance. Microbial limit test area was separated from all other microbiological activity (such as media preparation).

The reference cultures were purchased and aseptically hydrated with a ready media (GPT test was performed for each prepared media) in the laminar air flow benches, passaging activity was limited to maximum of 5 passages. Handling and storing of these culture organisms were controlled according SOP on standard practice in microbiology laboratory.

Microbiology laboratory equipment full set of data was available and was checked for calibration for balances, incubators, fridges, laminar air flow benches. Standard weights were externally calibrated according to the External calibration program.

Autoclaves: there were two separated autoclaves, one for the condemnation of the media and organism and the other one for the sterilization purposes. The annual validation report of the sterilization autoclave was reviewed, and no single data was out of limits.

SOP for cleaning of microbiology laboratory was reviewed the microbiology lab was cleaned daily using disinfectants.

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, ***Maphar Laboratories,*** located at ***Km 10, Route cotière 111, Quartier Industriel Zenata – Aïn Sebaâ, Casablanca, Marocco*** 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-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO TRS No. 986, Annex 2***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/
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 GMP for APIs*** or ***TRS No. 957, Annex 2***
   http://www.who.int/medicines/publications/44threport/en/

3. WHO good manufacturing practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-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 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 GPPQCL Guidelines or ***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 Gnneva, 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 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 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