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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	Mylan Laboratories Limited
Corporate address of manufacturer	House No 8-2-293/82/J — III, Plot No 564/A/22, Road No 92, Jubilee Hills, Hyderabad — 500034, Telangana, India.
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Plot No. P 1/6 of F10723, Lusaka South MultiFacility Economic Zone, Chifwema Road, Lusaka, Zambia
Inspection details	
Dates of inspection	12 to 16 September 2022
Type of inspection	Initial inspection (New Site)
Introduction	
Brief description of the manufacturing activities	The site was associated with the blister and bottle packaging (primary and secondary), testing and release of finished products (OSD). The manufacturing license was issued by the Zambia Medicines Regulatory Agency (ZAMRA). The site did not handle toxic, hazardous, mutagenic, teratogenic, substances, poisons, narcotics, hormones or veterinary products. The bottle line was unused since 2020 because of decreased market demand.
General information about the company and site	Mylan Inc., USA was founded in 1961 and has Corporate Headquarters at Pittsburgh, Pennsylvania, United States. Mylan Laboratories Limited is the Zambian Subsidiary of Mylan Inc., USA. The site's routine operation was reported to Mylan Corporate Office based in India. The site location is in a pollution free industrial zone (Lusaka South Multi facility Economic Zone) allotted by Government of Lusaka, Zambia. For MA099 Artemether/Lumefantrine Tablet 20mg/120mg, the primary and secondary packaging operation, the testing for incoming packaging materials and the physico-chemical testing for the finished product were performed on the site.
History	This was the first WHO pre-qualification on-site GMP inspection.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	– Quality management system – OSD packaging operations – Quality control laboratories (physicochemical tests) – Warehouses
Restrictions	The inspection was restricted to the production of the product listed in the inspection scope.

Out of scope	• Bottle line and bottle packaging • Stability testing
WHO product numbers covered by the inspection	MA099 Artemether/Lumefantrine Tablet 20mg/120mg
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
CNC	Controlled non-classified
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	Nonconformity
NCA	National control authority
NCL	National control laboratory
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

According to the organizational chart, the Quality Assurance was formally independent from the other functions like quality control, production, warehousing and engineering.

Product quality review (PQR):
The Product Quality Reviews (site terminology: Annual Product Review) were issued based on an annual schedule as required by the SOP for annual product review.
The APR of the Artemether/Lumefantrine Tablet 20mg/120mg (KOMEFAN) product for period May 2021-May 2022 was reviewed and discussed. The OOS, laboratory incidents, deviation, change control and CAPAs etc. were reviewed in the APR.

Quality Risk Management
The Quality Risk Management policy of Mylan Corporate was implemented according to an approved written procedure. The investigations and assessment related to the following topics were recorded.

- Packaging materials,
- Campaign length study,
- Delayed closure of CAPA,
- Indefinite closure of executed CAPAs
- Cross-contamination

Change Control

There were several change controls initiated in 2022 upon an approved written procedure. The initiated change controls were recorded in the registry. The change on the relocation of QC instruments within the QC laboratory was discussed.

Handling of deviations (incidents)
The deviations were handled according to an approved written procedure. The number of the investigated deviations in 2021 and 2022 were recorded in the logbooks. An incident case of failure to test stability samples in time because of an instrument breakdown (HPLC) was discussed.

Quality Management Review
There was a monthly reporting in place of key performance indicators together with the defined quality topics. The report was discussed amongst the group of experts including the corporate quality assurance.

CAPA
CAPAs were initiated following to investigations and other defined cases according to approved written procedure. The CAPA register for 2021 and 2022 were in place and checked. The CAPA upon implementation of an incident investigation form and the corresponding questionnaire-based training were discussed.

Batch Release
The Pharmacist-Quality was responsible for the release of the product before distribution according to the following several written SOPs and checklists.

Following the evaluations (particularly for the BPRs and quality control records) documented in the checklists, the "Certificate for Dispatch" document was prepared and signed by the warehouse manager and the Pharmacist-Quality.

2. Good manufacturing practices for pharmaceutical products

Good manufacturing practices were generally implemented. The manufacturing processes of primary and secondary packaging followed procedures as defined and documented in the BPRs. Adequate physical resources were provided to support packaging and testing operations. The procedures reviewed and discussed during the inspection were generally of an acceptable standard.

3. Sanitation and hygiene

Premises and equipment in the production area were maintained at a satisfactory level of cleanliness at the time of inspection. Personal hygiene and sanitation appeared satisfactory. Areas were cleaned frequently in accordance with an approved written programme.

The facilities were constructed in a way to assure the maintenance of proper hygiene conditions in the controlled areas. Toilets and the canteen were located in a separate facility. The facility cleaning procedures together with the checklists were available. The cleaning was performed by the production personnel supported by contract workers under the supervision of the permanent staff. The primary packaging facilities had different cleaning types which were recorded in cleaning checklists.

4. Qualification and validation

Validation master plan

The VMP was prepared according to SOP for preparation of VMP. The VMP required the following:

- Packing validation for the first three commercial batches.
- Cleaning validation.
- analytical method validation.
- equipment qualification.

The re-qualification was to be performed based on change control and periodic review. The procedure required VMP to be prepared at the beginning of each calendar year.

Process validation

The following process validation documents were available and reviewed.

- SOP for packaging validation.
- Packaging validation protocol for KOMEFAN (20/120mg Tablet).
- Packaging validation report for KOMEFAN. (Pack size 30x24's). The validation was done for Zambia market. There was a change control for initiation of PV for WHO grade product at the time of the inspection, and the PV has been completed after the inspection and addressed in the CAPA to an acceptable level.

Cleaning validation

The company claimed that the blister packaging line was dedicated to the product at the time of inspection. Therefore, only Lumefantrine and Artemether APIs were considered at cleaning validation of the blistering machine. The other products' packaging was operated with bottle lines. The following cleaning validation and cleaning procedure documents were available and reviewed.

- SOP for cleaning validation.
- SOP for cleaning procedure.
- SOP for operation and cleaning of blister packing machine.
- Protocol for cleaning verification of MA099 (KOMEFEN 140).
- Report for cleaning verification.

5. Complaints

The handling of complaints was managed according to an approved written SOP. There was no complaint recorded in the complaint logbook since the site started commercial production.
Theoretically, the complaints received are to be classified as critical, major or other. The critical complaints should be forwarded within specified time to the corporate (manufacturer of the finished dosage form) for investigation as per company's procedure. The monthly quality review (involving the site experts and the corporate QA) should serve as a forum of discussing the received complaints and their classification amongst other key performance indicators.

6. Product recalls

There was no product recall happened in the history of the site although the SOP was in place.

7. Contract production, analysis and other activities

There was no outsourced production contracted out by the site.

The water testing (chemical and microbiology) and the environmental monitory testing (microbiology) was contracted out to the Zambia Bureau of Standards, which is the local statutory body. The qualification of the laboratory by Mylan was based on an appropriate SOP and supported by an audit. The assessment form and the agreement between the Site and the Laboratory were available.

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

Annual self-inspection program covered the following areas:

- Quality assurance,
- Quality control,
- Packaging,
- Warehousing,
- Engineering

The last self-inspection was held in 2021 and the next one was due at the end of September 2022 according to the annual plan for year 2022.

All the raw materials and bulk products were received from Mylan affiliates. Accordingly, the main vendors of the site were considered as Mylan affiliates. The qualification of the "original" vendors/suppliers of the packaging materials was always performed by the affiliate. The list of approved vendors together with all the records related to the vendor qualification were provided by the affiliates and available. As such most of the provisions stated in the SOP regarding vendor qualification was related to the affiliates.

The main function of the site regarding vendor qualification was to report any deviation or vendor-related issue (incident) to the affiliate triggering re-qualification of the concerned vendor. The approved vendor list together with the vendor approval records of the supplier of the PVC were discussed.

9. Personnel

The organizational chart was issued and controlled as an attachment of the actual SMF. The personnel of the site were as follows:

Production (including the head of site operations, warehousing, packaging, engineering)	6 persons
Quality Assurance and Quality Control	4 persons
Contract workers	12 persons

The main responsibilities, tasks, reporting and substitution of the permanent staff were described in job descriptions. The job descriptions of all permanent staff were available, namely:

- General manager operations,
- Pharmacist-Quality,
- Warehouse manager
- Engineer manufacturing
- QC Analyst/QC officer
- Technician manufacturing

The Mylan affiliates and Mylan Corporate provided support to the site in the following areas:

- Human resources
- Supply chain including the generation of product codes
- Regulatory affairs
- Engineering
- Quality control and stability testing program
- Preparation of product quality reviews
- Investigation of incidents
- Handling of authority inspections
- Analytical method transfer
- Technology Transfer (Packaging)
- Preparation of Batch Packaging Records
- Management review
- Training
- Vendor qualification
- Preparation of SOPs

There was a technical and quality agreement in place between the site and the affiliates (Mylan Indore, Mylan Nashik). It stated that the Mylan Zambia site does not test and release bulk tablets.

10. Training

The training program of the staff was managed according to an approved written procedure.
The newly hired staff undergo induction and ongoing trainings including the general introduction of the company, the concerned SOPs and the GMP sections, provided by a trainer with proper expertise.
The training and training evaluation records were available.

11. Personal hygiene

There was a provision in place that personnel entering the facilities including permanent staff, contract workers and visitors should follow the gowning procedure.
The procedure described the dressing code to be followed in the controlled and uncontrolled areas. The same was indicated on the wall in the primary and secondary change rooms.

12. Premises

The premises were new, constructed less than 5 years ago. Areas for primary and secondary packaging and storage of materials had adequate space for the appropriate performance of activities. The material and personnel flow were defined to prevent mix-ups.

The walls and floor were non-porous, smooth, washable without crevices, recesses, protrusions, or joints.
By function, the following main areas were defined in the production areas and visited during the tour:

- CNC corridor
- Blister packaging line, primary
- Bottle packaging line, primary,
- Secondary packaging area (common for blister and bottle)
- Primary packaging material and bulk tablet storage

- Finished product storage
- Secondary packaging material storage
- Primary and secondary change rooms
- IPQA room
- Washing rooms

The access to the quality control laboratory was through the uncontrolled corridor of the production areas.

The primary packaging area was classified as ISO Class 8. AHUs in the controlled areas were re-circulatory type. Terminal HEPA filters were provided in process areas. Process corridor was positively pressurized with respect to process rooms. The primary packaging area was positively pressurized to ambient pressure secondary packaging areas.
The qualification of the Blistering Room and the AHU supplying the area were discussed. The drawing of the AHUs and the layouts of the facilities indicating the classification and the pressure differences were available. The initial qualification and requalification of the system were recorded and checked. The AHUs were operated according to an SOP.

13. Equipment

The equipment and instrumentation were new and mainly imported from India. The department-wise list of equipment containing the function, ID and location was available. Apart from the master list, there were separate annual calibration and maintenance scheduler prepared indicating the previous and due events.

Equipment qualifications, calibration and maintenance
The qualification documents including URS, DQ, IQ, OQ, PQ of the Blistering Machine were discussed. The calibration records of the measuring devices attached to the blistering machine were available. The preventive maintenance of the blistering machine was performed according to the documented protocol and recorded on the preventive maintenance checklist. The event of the maintenance or repair was logged in the instrument logbook.

Water System
Two different quality water was used in the production facilities and the QC laboratory:

- Tap water: for general cleaning
- Purified water for cleaning (final rinsing) and analysis

The purified water was generated by Merck Millipore, Elix 100 to deliver water quality of desired specification for usage in the laboratory and in the cleaning of production equipment /areas. The purified water was transferred from the Millipore to the manufacturing areas in two SS vessels.
The quality of the water was stated in the approved specifications. The quality of the water was tested by the QC laboratory (chemical tests) and quarterly by a contract laboratory (microbiology). The test results were trended, the trend analysis for the year 2021 was available.

14. Materials

The materials were handled according to SOPs covering the whole route within the company starting with the material receipt and ended with the dispatch.

The materials received from outside were dedusted then placed into the concerned part of the warehouse. The main data of the material receipt were recorded in the inward register. The warehouse manager was responsible for receiving the materials and the accompanying documents according to the Material Receipt Checklist. The location of the materials in the warehouse were indicated in "Bin-cards".
There were Goods Receipt Notes (GRNs) prepared for each shipment and batch of materials entering the warehouse, subject to sampling (as primary packaging materials, secondary packaging materials, finished products). The shipment, receipt, storage and release records of PVC and two batches of KOMEFAN 20/120mg Tablet were discussed.

The warehouse was responsible for dispatching commercial goods only after batch release, properly labelled and palletized according to approved SOPs.

The materials (including packaging materials, intermediates, finished products) were identified by two different product IDs:

- SAP code for marketing purposes,
- Product code for GMP procedures.

The product codes were generated at the Mylan corporate level. The quality of the material was stated in the product quality specification document together with the corresponding Standard Testing Protocol (STP) defining the details of the test methods.

The finished products were assigned a batch number, generated, recorded and indicated according to the "SOP For Assigning Batch Numbers for Finished Product."

15. Documentation

The documentation system was paper-based and controlled by QA department. In general, documentation was designed, prepared, reviewed and distributed according to approved written procedure. The master copy of the documents was stored in the "Document Store" for a period defined in the SOP. Access to the archive was restricted by a door lock openable through an e-card reader. The documents had unique IDs generated upon the "Document Numbering System."

Despite there being no electronic data handled at the site (apart from the QC data), there was an SOP available for computerised system handling and validation. The backup of electronic data from production, warehouse and engineering was also regulated. The SOP for conducting stability studies, and SOP for Management of policies, privileges, data and users in software application was followed for used management in the Water HPLC systems.

16. Good practices in production

Inspectors visited all production areas and observed the following activities amongst others:

- Warehousing: semi-finished goods (bulk tablets), primary & secondary packaging components,
- Labeling components and finished goods.
- Sampling: primary and secondary packaging components and finished drug product.
- Dispensing: packaging components and bulk tablets
- In-process testing lab (IPQA Lab) and quality control lab
- Packaging line for blisters and bottles

At the time of the tour the blistering and secondary packaging of KOMEFAN 20/120mg Tablet was ongoing. The blistering machine was operated using the PLC, also indicating the setting and actual operating parameters. The manufacturing activities were recorded in batch packaging records. The batch packaging record of the batch under packaging was available in the processing area. The BPR was reviewed.

Reworking and reprocessing
A SOP for reprocessing and reworking was implemented. Any reprocessing/reworking taking place was performed and documented strictly in accordance with this procedure.

17. Good practices in quality control

The quality control laboratory was responsible for the sampling and testing of packaging materials, finished products, stability samples (not for WHO), purified water (physico-chemical testing only) and the managing of the retention samples.

The premises of the microbiology laboratory were available and built with a mobile LAF and AHU, however there was no activity taking place at the time of the inspection due to a lack of instruments and appropriately qualified personnel.

The incoming samples were recorded in the AR register and AR numbers was generated based on the 'goods receipt note' (GRN) for packaging materials and 'Finished Product Analysis Request' for the finished product.

The main instrumentation of the laboratory included the following:
- Semi-micro balance
- KF titrator
- PH/Conductivity meter
- Ultra-micro balance
- UV/VIS spectrophotometer
- HPLC
- Dissolution tester
- TLC photo document chamber
- IR spectrophotometer
- Disintegration tester
- Friability tester
- Breaking-force tester

QC analysts perform the sampling of incoming packaging materials as per the sampling SOP and affixes the "Sampled" label.

The reference materials were stored in ambient or cold 2-8 ^{0}C temperature. The records of Artemether RS and Lumefantrine RS were available in the reference standard register and the reference standard usage record.

The retention samples were stored under controlled temperature. The retention samples were spot checked.

The site had a general instruction in-place on good chromatographic practice. The user privileges of the HPLCs were managed upon an SOP for the operation of HPLCs. Analytical equipment was regularly qualified and maintained. The HPLC calibration, qualification and maintenance records of HPLCs checked were available and discussed. The maintenance program for year 2022 was prepared according to an SOP and the specified form. The maintenance of the HPLCs were performed by the supplier or the site engineers according to the documented protocol.

The analytical test procedures (STPs) used by the company were developed by the site of formulation then transferred to the site in the framework of formal analytical method transfer. According to the SOP, the protocol is to be prepared by the donor site. The method transfer study of protocol and report of analytical test methods used for KOMEFAN 20/120mg Tablet, the quality specification, STP and the test records of KOMEFAN 20/120mg Tablet (3133181P1) were discussed.

The out-of-specification (OOS) results were reported and investigated. Several OOS events were recorded in the laboratory investigation register for 2021 and 2022. The case of a failed lumefantrine assay was discussed. Following to the stage I and stage II investigations, the study concluded the OOS result invalid.

The stability program was defined in an approved written SOP.

Part 3	**Initial 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, ***Mylan Laboratories Limited***, located at ***Plot No. P 1/6 of F10723, Lusaka South MultiFacility Economic Zone, Chifwema Road, Lusaka, Zambia*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines for packaging and physicochemical testing of solid oral dosage forms.

All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the WHOPIR, were addressed by the manufacturer, to a satisfactory level, prior to the publication of the WHOPIR.

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

Part 4	**List of GMP Guidelines referenced in the inspection report**

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eight Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO TRS No. 986, Annex 2***

https://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***
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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**
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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**
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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**
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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***
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