

**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	Mylan Global Centre, Bangalore: 9th Floor, Prestige Platina 3, Prestige Tech Park II, Outer Ring Road, Kadubesanahalli, Bengaluru-560087, Karnataka, INDIA ☎: +91-080 - 66728000 📠: +91-080 - 66728899	
Inspected site		
Name & address of inspected manufacturing site if different from that given above	Mylan Hosur Steriles Facility Plot No. 13 A, 14 & CP 2, SIPCOT Phase - II, Krishnagiri Main Road, Hosur- 635130, Tamil Nadu – India Data Universal Numbering System (DUNS) number: 65-065-8052 Facility Establishment Identifier number: 3008255419 GPS Details: 12°43'48.1"N 77°51'47.9"E	
Unit / block / workshop number	Hosur Steriles Facility (HSF)	
Inspection details		
Dates of inspection	10-14 June 2019	
Type of inspection	Routine GMP inspection	
Introduction		
Brief description of the manufacturing activities	Mylan Laboratories Limited is a fully owned subsidiary of Mylan N.V. The Hosur Steriles Facility located at Hosur, Tamil Nadu, is used for the manufacture and distribution of a wide range of sterile pharmaceutical products. The Hosur Steriles Facility (HSF) was acquired by Mylan from Agila Specialties Pvt. Ltd. in 2013 (effective from 5 th Dec 2013) which had acquired the facility from Star Drugs and Research Labs in 2012 and renamed it as Hosur Steriles Facility (HSF). After the acquisition, a facility renovation had been performed in a phased manner. Changes were made to Facility, Equipment and procedures aligning them with the quality policies of Mylan Laboratories Limited. The HSF facility had the Administrative block, Quality Control and Microbiology on the First floor and Manufacturing, Compounding, Filtration and Filling areas on the Ground Floor level. Packing and Finished Goods stores were located in the Basement. The Complex Injectable Facility had a separate Raw Material Store, Manufacturing & Filling	

	<p>suites which were being commissioned. The total area of the site was about 3.9 acres with the built-up area about 19000 sqm.</p>
<p>General information about the company and site</p>	<p>This facility is engaged in manufacturing of sterile medicinal drug products (Parenteral and Ophthalmic) for human use and is licensed to manufacture the following dosage forms:</p> <ul style="list-style-type: none"> ✓ Liquid Parenterals in Vials ✓ Liquid Parenterals in Ampoule ✓ Liquid Parenterals in Pre-filled syringes ✓ Lyophilized (Freeze Dried) ✓ Liquid Ophthalmic Products ✓ Dry powders for injection <p>The manufacturing facility has been approved by Drugs Control Authority Tamil Nadu State (located at Chennai), India. The drug manufacturing license number: TN00003234 (for the manufacture of small volume Parenteral). The facility is certified to meet the WHO standards by the National Regulatory Authority as well as approved by US FDA. Products are manufactured on Campaign basis.</p>
<p>History</p>	<p>The site was last inspected by the WHO PQ Team in January 2017. In addition, the following authorities had inspected the facility within the last three years:</p> <ol style="list-style-type: none"> 1. USFDA, USA 16-24 May 2019 2. CDSCO, INDIA 23 April 2019 to 24 April 2019 3. TFDA, Taiwan 15 Apr 2019 to 19-Apr 2019 4. USFDA, USA 08 May 2017 to 15 May 2017
<p>Brief report of inspection activities undertaken – Scope and limitations</p>	
<p>Areas inspected</p>	<ul style="list-style-type: none"> ○ Pharmaceutical Quality System ○ Documentation system ○ Material management system ○ Production Block and production system ○ QC Laboratory: Chemical and Physical Lab, Microbiology laboratories ○ Validation
<p>Restrictions</p>	<p>Products and/or other process areas outside of the WHO pre-qualification programme were not inspected.</p>
<p>Out of scope</p>	<p>The scope of the inspection was restricted to the sterile FPP i.e. TB329 in the WHO PQ program. The inspection of the production area only covered the so called “Combi-Line”. Whilst this line has the capability for the filling of three-part plastic eyedrop containers, these products were out of scope.</p>
<p>WHO products covered by the inspection</p>	<p>Capreomycin powder for injection 1.0gm (TB329)</p>

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

A formal documented system of quality assurance was established, with procedures covering key quality elements being in place. QA and QC departments were independent of production. Operations were specified in written form and GMP requirements were essentially being met. The procedures that were reviewed and discussed during the inspection were generally of a satisfactory standard. Product and processes were monitored, and these results considered during batch release. Regular monitoring and reviews of the quality of APIs and FPPs were being conducted according to documented schedules and procedures.

Product quality review

PQR procedure was discussed. The procedure applies to all commercialized drug products, which includes review of batches manufactured during the review period at a manufacturing site. A PQR schedule / planner was required to be prepared in the month of December by the site QA coordinator for APR/PQR for the following calendar year. This schedule was available and reviewed. The procedure was supported with a flow chart, templates for the PQR report, planner and template for identification of critical quality attributes and critical process parameters.

There had been no commercial production and was no PQR available for Capreomycin powder for injection 1gm.

Change management system

The company had a SOP which described the process for initiating permanent and temporary changes. It listed the responsibilities and requirements for the management of cGMP changes having a regulatory and having no regulatory impact and to tracking for effectiveness where applicable. The SOP covered procedures to be followed for both regulatory and non-regulatory impact changes related to master document, processes, equipment(s), facility, utilities or systems of Hosur Steriles Facility. The electronic QMS was being used for the handling of change management and other quality system elements. In general, the procedure was found adequate and was supported with typical examples of key quality impacting changes that may require quality risk assessment.

Batch release

Result recording, usage decision making and disposition of raw materials, semi-finished goods & finished goods) was discussed. The procedure was applicable for review of executed BHR (Batch History Record). The BHR included the BMR (Batch manufacturing Record), BPR (Batch Packing Record), QC (Quality Control) and Microbiology analytical records and associated attachment's as applicable, and all printouts associated with the manufacturing, packaging process prior to Semi-Finished Goods (SFG) and Finished Goods (FG) disposition at HSF. This procedure was supported by several more detailed sub-procedures such as those for finished goods release, and the SOP for review of QC results. In general, the procedure was adequate except that clear responsibility and frequency for the review of source data was not specified.

Quality risk management/QRM:

A procedure on performing risk assessment was in place. The procedure covered the drug product life-cycle approach where risks were proactively identified, responsibilities were documented and appropriate actions were identified for implementation. Failure modes and effects analysis (FMEA) was the preferred tool for conducting most risk assessments performed in the company. Other applicable tools were also described. The procedure was supported with templates for QRM protocols and risk-based prioritization planning. In general, the procedure was found adequate.

Corrective and preventive action (CAPA) management system

A procedure was in place which described identification & evaluation, review, tracking and implementation of CAPA. This was a site specific procedure which covered the tracking of CAPA identified for implementation during site investigations from incidents, deviations, complaints, recalls, PQR, QRM, OOS, OOT, internal and customer audits, regulatory inspections and non-conformances. The electronic QMS had been configured and was used for handling, tracking and trending of CAPA and its effectiveness check. In general, the procedure found adequate and did not rise to any significant concerns.

Contamination control strategy

Based on the draft revision of WHO/EU/PICs sterile GMP, Mylan’s corporate team had prepared a presentation for the implementation of the recommendations in the revision. Some work has already been initiated to correct gaps identified, e.g. a quality risk assessment and management process for “cross contamination and mix-ups” had been initiated and was being rolled out to corporate sites. The document delineated methodologies to identify the associated risks, existing controls and mitigation actions, if any, due to manufacturing of different categories of molecules with respect to cross contamination. The process flow chart provided an overview of the areas (facility design flow, personnel/material movement, gowning/gloves, cleaning, labelling and HVAC etc.) that are considered for identifying potential areas of cross contamination and mix-ups. The FMEA tool had been used for assessing risk and risk priority number were derived for each risk factors/elements and assessed against the acceptance criteria.

The issues noted from this section have already been addressed and will be verified during future inspections.

2. Good manufacturing practices for pharmaceutical products

Good manufacturing practices were generally implemented and followed. Manufacturing processes were defined and documented. Qualification and validation activities generally had been performed. Manufacturing steps were recorded in batch manufacturing and packaging records and associated manufacturing SOPs. Product was released by named authorized persons.

Manufacturing processes of capreomycin powder for injection, was reviewed and discussed.

The issues noted from this section have already been addressed and will be verified during future inspections.

3. Sanitation and hygiene

Premises and equipment were maintained at an acceptable level of cleanliness. The company had a standard operating procedure in place as the basis for its approach to personal hygiene and sanitation in production facilities. There were procedures in place for the preparation and rotation of sanitation solutions used in production. Gowning policy is followed in all areas. In general, the operators presented an adequate level of aseptic practice and the number of interventions into the production class A critical zones were limited during the periods of observations which included both line set up and running of the aseptic connections and filling operations

4. Qualification and validation

A high-level validation master plan and policy was in place which was stated based on corporate documentation and applicable to all injectables sites of Mylan Laboratories Ltd India. The VMP described the intentions and approach of Mylan Laboratories Ltd towards validation in achieving the validation policy and the objectives of providing products meeting the relevant predetermined quality attributes. The VMP covered the following programs:

- facilities and equipment
- utilities (e.g. water system, HVAC)
- computerised systems used for GMP activities
- manufacturing process including cleaning and aseptic process
- analytical and microbiological methods
- transportation
- additional validation/qualification activities (e.g. temperature, RH, mapping etc.)

The inspection team reviewed the sterility testing isolator requalification, media fill simulations and smoke studies.

The issues noted from this section have already been addressed and will be verified during future inspections.

5. Complaints

Management of drug product complaints was in place and reviewed. The procedure was applicable to all products distributed that are manufactured at Mylan's Hosur sterile facility. The complaints were logged and tracked and documentation handled through the electronic QMS. In general, the procedure was found adequate.

6. Product recalls

The SOP on product recall was in place. No specific issue was noted with the procedure and was found adequate.

7. Contract production, analysis and other activities

Production of Capreomycin powder for injection was not contracted out. Mylan had in place contracts with analytical laboratories.

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

The internal site quality audit (self-inspection) procedure was in place. This procedure was applicable to internal quality audits performed at site by the site personnel. The internal quality audits were performed at least once in a calendar year and based on the traditional six system approach, covering the quality system, laboratory control system, production system, packaging and labelling system, facilities and equipment system and materials management system. The internal quality audit observations were classified into level 1 (critical), level 2 (major) and level 3 (minor). In general, the procedure was found adequate.

In addition, the company has a programme of corporate audits.

9. Personnel

The manufacturer had an adequate number of personnel with the necessary qualifications and practical experience. Personnel interviewed during the inspection were aware of the principles of GMP with experience for sterile product manufacturing. An organization chart was available and considered acceptable. The following number of staff are engaged as noted from the site master file as well as from the opening meeting presentation:

S. No.	Department	Total	S. No.	Department	Total
1.	Manufacturing Operations	252	2.	Stores (Warehouse)	18
3.	Quality Assurance	60	4.	HRA	6
5.	Quality Control	61	6.	EHS	7
7.	Microbiology	41	8.	Planning	01
9.	Engineering	55	10.	CSV	01
11.	Security	2	Total Employees		509
12.	Validation	5			

The issues noted from this section have already been addressed and will be verified during future inspections.

10. Training

Training needs are identified by the respective department Heads. An annual training plan is prepared along with the Head-HRA for each employee according to his/her position and nature of the job. After imparting the necessary training, an evaluation is carried out with respect to “awareness”, knowledge and “competence” which it was explained meant skill on the job by the department head and Head-HRA. All the training was managed through IT enabled software (LMS-Learning management system).

The SOP for visual inspection by manual method described the procedure for 100% manual inspection including the light intensity (lux measurement) and cleaning of the manual inspection tables. The visual inspections are performed by the production operators whereas AQL inspections are performed by the QA staff. Qualification of inspectors was identical for both production and QA operators. In addition, a second procedure was in place for manual inspection of lyophilized vials. Classification and limits for visual inspection rejects were described in the procedure. Defects were categorized as critical defects, major defects and minor defects, with acceptance limits established for each category. It was confirmed that an eye test was performed once every 6 months when operators were sent to eye specialist (ophthalmologist). It was recommended to invite the ophthalmologist on-site and show them the kind of work operators were involved into.

The microbiologists were requalified once every two year, there was however no documented justification available for the requalification.

The issues noted from this section have already been addressed and will be verified during future inspections.

11. Personal hygiene

Changing and washing before entry to production areas followed written procedures. Direct contact was avoided between the operator's hands and starting materials, primary packaging materials and intermediate or bulk product. The protective clothing washing and sterilization operations followed standard operating procedures.

12. Premises

Exposed surfaces in the production areas of the injections workshop were generally smooth, impervious and unbroken.

The powder and liquid injection production lines used for WHO PQ FPPs were not dedicated to capreomycin. There were several different products produced on the powder injection line and small volume liquid injection lines.

Change rooms were designed as airlocks and used to provide physical separation of the different stages of changing. Change rooms were flushed with filtered air. The final stage of the changing room was at the at-rest state grade as the area to which it leads. Changing rooms were equipped with mirrors.

Aseptic operations were performed in class A area with class B background. All relevant drawings (clean room classes, pressure room pressure, personnel flow, material flow) were available. Manufacturing and packaging operations are done under the classified facility according to WHO guidelines with validated machines and processes.

Separate air handling units (AHUs) were provided for the liquid vial, dry powder, lyophilized injection sections and for the QC analytical and microbiology department. The air handling systems were provided with the pressure balancing arrangement to mitigate possible cross-contamination risks between the products. The core processing areas e.g. filling area were designed as grade A with grade B background. The temperature and RH were maintained as per the requirement of the process and activity performed. Centralized dehumidifiers were provided in the area where low relative humidity was required. Air Changes for each room were designed as per the requirement of the process and the activity performed. Differential pressure between different areas was specified to avoid any cross contamination.

Storage areas for starting materials and finished products were visited. Finished products warehouse were packed. WHO products were kept in a room within the secondary packaging area.

The issues noted from this section have already been addressed and will be verified during future inspections.

13. Equipment

The equipment inspected in the production area was generally appropriately installed and of an acceptable standard. The filling line was designed using grade A in the grade B background environment. The filling lines for powders (vials) and ampoules, included in-line washing machines, sterilizing and depyrogenation tunnels, and filling and sealing machines were installed in separate suites. The filling line for capreomycin is a combi-line which is also adaptable for the filling of three part plastic eye drop containers.

14. Materials

The raw materials and packaging materials were received from the approved source only. Source approval and source evaluation procedure was in place. Materials were stored as appropriate to their storage conditions. Rejected and waste materials were handled carefully as per SOP.

The materials were purchased from approved source. Approved Sources were maintained through SAP. Quality agreements with the manufacturers were maintained. Risk based yearly Audit plan was in place.

Materials were received, sampled and tested according to the written procedures.

15. Documentation

Documentation was prepared, authorized and distributed according to written procedures. SOPs and controlled log books were kept which generally allowed traceability. BMRs were retained for each batch processed. Batches were numbered according to a written procedure.

16. Good practices in production

Non-sterile capreomycin Sulphate API is supplied by the API manufacturer in a sealed bag. The non-sterile API was used to prepare the solution prior to filtration and aseptic filling into, lyophilized and sealed.

At the time of the inspection, product in scope was not running. It is understood that the company had not received any order for Capreomycin powder for injection from any stakeholder who uses WHO PQ in its procurement protocols. The company demonstrated the manufacturing process by filling water for injection into vials as a “placebo”/engineering lot. The machine set up for the Combi filling machine was inspected and found generally acceptable with a small number of observations made where the company should consider alternative approaches with the aim of further mitigation of aseptic and extrinsic particulate risk. For Grade A and B zones, particle monitoring was undertaken for the full duration of processing, including equipment set up and assembly. The microbiological cleanliness of Grades A–D in operation in the clean areas was generally in accordance with the GMP recommendations and monitored with alert levels set which were derived from trend data.

The processes inspected was generally well designed so as to protect the product from extrinsic contamination risks to products whilst also maintaining protection for operators. BMR, BPR & Batch numbering system was followed in production with only limited documents being taken into the manufacturing area and records being kept remotely where practicable. Line/area clearance procedures were in place before starting a new production batch. Review of EM trend data indicated that appropriate room conditions were being maintained during production. In-process quality controls were performed during production.

Inspection and packaging was reviewed and generally found to be acceptable but was only spot checked during this inspection.

The company inspects the lyophilised products using visual inspection systems supplemented by an X-ray system that has a capability to detect dense particles that would otherwise have a very low likelihood of detection by manual or automated visual examination alone. For liquid products the company also uses automated systems but this equipment is not used for the PQ product and therefore not inspected.

The SOP for cleaning and operation of x-ray inspection system was reviewed and was applicable for the inspection of lyophilized products and dry powder products. The procedure described a routine machine challenge test using a standard contaminant (The test set consisted of aluminum ball, ceramic ball, SS wire, glass balls and SS balls varying sizes of 0.5mm to 2.0mm). The approach to verification was similar to the approach used by the company for their “KNAPP” sets for visual examination qualifications and routine verifications.

The issues noted from this section have already been addressed and will be verified during future inspections.

17. Good practices in quality control

The quality control laboratories were well separated from production areas. The general and microbiology QC laboratories were inspected. Since the last WHO PQ inspection in January 2018, the quality control laboratory had been expanded.

The chemistry laboratories were equipped with a total of 19 HPLC system of different make and all were networked and running with electronic software for data acquisition. Data were reviewed by both quality control and analytical quality assurance who in turn report to quality assurance.

The 36-month stability study of Capreomycin powder for injection had been completed. The source data were verified during inspection. Upon review of these electronic data, it was noted that adequate controls were lacking in some instances where integration privileges allocation to various test personnel without thorough review, potential adverse impact and documented justification.

Environmental monitoring

The microbiology team was responsible for trending of viable monitoring whereas production personnel are responsible for non-viable particle counts (NVPC).

Microbiological evaluation of clean rooms and other controlled environments was set out in SOPs and were discussed. Environmental monitoring was performed using settle plate, air sampling, surfaces (contact plate and swabs) and personal monitoring was performed using glove and gown plates.

Continuous particle monitoring system

Operation of the continuous particle count monitoring system was discussed. The system and procedure was applicable to all three lines (vial line, combi line and ampoule line) and covered the monitoring of both Grade A and B areas. A network-based application was used for continuous particle count data acquisition monitoring. Audio and visual alarms were provided inside the production area which prompt production operators to stop the activity.

Out of specifications (OOS)

The company has procedures for handling OOS and OOT results that are mature in content and implementation. The OOS investigations reviewed during this inspection raised no serious matters of concern.

The issues noted from this section have already been addressed and will be verified during future inspections.

Part 3	Conclusion – Inspection outcome
---------------	--

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, *Mylan Laboratories Limited*, located at *Hosur Steriles Facility, Plot No. 13 A, 14 & CP 2, SIPCOT Phase - II, Krishnagiri Main Road, Hosur- 635130, Tamil Nadu – 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-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. Fourth-Sixth Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2
Short name: WHO TRS No. 970, Annex 2
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/
4. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-Ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4
Short name: WHO TRS No. 929, Annex 4
http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

5. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8. **Short name: WHO 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 Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 3. **Short name: WHO TRS No. 992, Annex 3**
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf
18. WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4. **Short name: WHO TRS No. 992, Annex 4**
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf
19. WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5. **Short name: WHO TRS No. 992, Annex 5**
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

20. WHO Recommendations for quality requirements when plant – derived artemisinin is used as a starting material in the production of antimalarial active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 6
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