

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

Part 1	General information
Manufacturers details	
Name of manufacturer	Beximco Pharmaceutical Limited
Corporate address of manufacturer	19 Dhanmondi R/A, Road No: 7, Dhaka-1205, Bangladesh
Inspected site	
Name & address of inspected manufacturing site if different from that given above	126, Kathaldia, Auchpara, Tongi-1711, Gazipur, Bangladesh GPS coordinates: 23.9030049, 90.3912181 DUNS No: 73-157-9053
Unit / block / workshop number	OSD Unit, Track-2
Inspection details	
Dates of inspection	10 – 12 March 2020
Type of inspection	Routine re-inspection
Introduction	
Brief description of the manufacturing activities	Production and quality control of • Oral Solid Dosage • Ophthalmic • Metered dose inhaler, dry powder inhaler (MDI & DPI) • Liquid, Cream, Ointment & Suppository • SVP and Nebulizer • Intravenous Fluids • Lyophilized and Prefilled Syringe Injectable • Insulin • API
General information about the company and site	Beximco Pharmaceutical Limited is situated in Tongi Industrial Area, Gazipur, approximately 25 km north of Dhaka city. The administrative head office of Beximco is in the Dhaka city. There were three Tracks on the site: Track 1, Track 2 and Track 3. Track 2 in the inspection scope has four sections: OSD unit, MDI unit-I, MDI unit-2 and DPI.

	FPP products including Penicillin and Cephalosporin products were managed by Track 1. The company stated that Cephalosporin products were manufactured by third parties via CMO contract manufacturing and Penicillin products were manufactured in a penicillin dedicated facility, 10 km away from Tongi, Gazipur.
History	This report presents the second WHO inspection of the site with the first inspection 7 - 10 February 2017. Track 2 OSD had been inspected by Malta Medicines Authority in 2019, TGA in 2018 and US FDA in 2015 with positive outcomes. The site is inspected by the Directorate General of Drug Administration (DGDA) Bangladesh on a regular basis.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	• Quality management system • OSD production block, Track 2 • QC including chemical and microbiological laboratories • FG Warehouse of Track 2 • Stability study area • FG sample retention area
Restrictions	The inspection was restricted to the product listed in the inspection scope.
Out of scope	Products and production areas outside of the inspection scope were not inspected.
WHO products covered by the inspection	HA 668 - Lamivudine Film-coated Tablets 300mg
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
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1. Pharmaceutical quality system

The quality system of multiple manufacturing Tracks in the company was not harmonized with each Track implementing its own quality system. For Track 2 in this inspection scope, the quality management system was generally established, documented and implemented. Quality-related activities were defined and documented. The quality department functioned independently from the production department. The persons authorized to release products were specified.

Annual Product Quality Review

The company had in place a procedure for performing product quality reviews. The SOP presented a general description for APQR and included the purpose, scope, responsibility and procedure. APQRs are performed annually for the period January to December.

The PQR 2019 for WHO grade Lamivudine tablets 300mg was reviewed. Three process validation batches of Lamivudine tablets 300 mg were produced in 2017. No commercial batches of WHO grade Lamivudine tablets have been supplied to market since the product being qualified. Non-compliances observed during the inspection were listed in the full report regarding the PQR. These were addressed by the manufacturer to a satisfactory level.

Quality Risk Management

The risk assessment procedure was reviewed and found acceptable. Revised QSM report for manufacturing of Lamivudine 300mg tablets in OSD Track 2 was reviewed. The potential risk for Track 1 products being manufactured and stored in Tack 2 facilities were discussed and was addressed by the manufacturer to an acceptable level.

Deviations, OOS and Non-Compliance Management

Procedures for management of Deviations, OOS and non-compliance were established and recorded in the appropriate register for OSD and included all products. The current review focussed on the WHO grade Lamivudine tablets.

Deviations

The SOP for deviation management was reviewed. The procedure defined what a deviation is, being planned or unplanned and three classification levels, critical, major and minor based on the impact analysis. The procedure also allows for immediate action that can be initiated. Deviation Register for 2017 was checked for deviations of lamivudine Batch manufactured. The deviation procedure was followed and subsequent CAPAs described.

Incidents

The company had a procedure to list events as incidents with a separate register. These incidents were reviewed and may be re-categorised as OOS. QA is responsible for assessing the event reported via head of QC and issue the incident log number.

OOS management

The OOS events reported showed that grouping the root causes it appears that “analyst error” is a major contributor leading the OOS events. The company had a procedure allowing for root cause investigation applying the fish bone analysis. Two OOSs of lamivudine tablets stability testing were reviewed. Non-compliances observed during the inspection were listed in the full report regarding OOS investigation. These were addressed by the manufacturer to a satisfactory level.

CAPA:

The CAPA procedure and the OSD CAPA Register 2019 were available for review. The CAPA based on the deviation during tablet compression was reviewed and discussed. Non-compliances observed during the inspection were listed in the full report regarding CAPA were addressed by the manufacturer to an acceptable level.

Change Control

Change controls for impurity and residue solvents testing of Lamivudine API was reviewed. The study for the testing method was contracted to external laboratory and was ongoing at the time of inspection.

Product Release

Product release was managed according to a documented procedure. QA is responsible for the final review of all the relevant documents including BMR, BPR etc. according to the SOP. A checklist was used and had to be completed in the final review. No commercial batches of WHO Lamivudine tablets 300mg has been distributed to market since it has been qualified.

2. Good manufacturing practices for pharmaceutical products

Good manufacturing practices were generally implemented. Necessary human and physical resources with adequate premises, equipment and utilities were provided for the current operational level of FPP activity. Manufacturing processes were adequately defined. The manufacturing processes followed procedures as defined and documented in the BMRs and BPRs. The personnel were appropriately qualified and adequate training was conducted.

3. Sanitation and hygiene

Entry into the manufacturing area was controlled with card access. The company followed adequate sanitation procedures upon entering the production facilities, which included a primary step-over, with shoe covers and hand washing procedure followed by gowning procedure.

Premises and equipment were generally clean. Change rooms were well maintained, and instructions displayed for gowning available. The company has procedures in place with relevant pictorials in the facilities to guide personnel. QC laboratory was equipped with health and safety equipment for events involving eye injury and spilling.

The company has a process in place for yearly health screening for all staff. Eye checking is performed on all staff members involved in responsibilities which include inspections e.g. inspections of tablets.

4. Qualification and validation

Validation master plan

An approved VMP was available and reviewed. The company qualification and validation policy and programme was defined and documented.

Process validation

Process validation was performed according to a validation procedure. The process validation protocol and report of HA 668 Lamivudine Film-coated Tablets 300mg as well as BMRs of PV batches were reviewed. The process validations were generally acceptable.

Cleaning validation

The approach to cleaning validation mentioned in VMP reviewed was acceptable. Cleaning validation was not reviewed in detail due to time constraint.

Computer System (CS) validation

Computerized systems were used in the material management, production, BMS and QC laboratory in Track 2. HPLC and GC was networked, and the company had basic systems on data integrity controls in place.

Production equipment was linked to PLC systems and pre-programmed recipe-based. The data integrity including access control and audit trail of a granulator was spot checked and discussed during the inspection. The CS validation was not reviewed in detail due to time constraint.

5. Complaints

The company had a complaint management procedure in place. Complaints register for 2019 and 2020 were maintained. The summary of product complaint handling was documented, and spot checked. No commercial WHO grade Lamivudine tablets 300mg batches have been supplied to market and no complaint was therefore reported.

6. Product recalls

The SOP for product recalls was checked. The procedure covered general recall requirements with a flow chart directing actions in the event of a recall. Recall simulations were required to be performed per the SOP for both domestic and export markets. The recall simulations were not reviewed in this inspection due to time constraint.

7. Contract production, analysis and other activities

The production for the WHO grade Lamivudine tablets 300mg in the inspection scope was not contracted. Pest control is conducted and was performed by an external contractor.

Some testing for the Lamivudine API was contracted to external laboratories. The technical agreement and method transfer were checked. Non-compliances observed during the inspection were listed in the full report relating to contract testing. These were addressed by the manufacturer to a satisfactory level.

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

Self-Inspection

The company had a procedure in place for self-inspection which had three components, namely the SOP, self-inspection report and self-inspection response. The company performs self-inspections with the QA as leader with co-auditors on a regular basis. QA initiated the training of staff based on the outcomes of the self-inspection. Report of self-inspection approved in November 2019 reviewed found that the procedure was adequately followed.

Supplier audits

The qualification of the Lamivudine API supplier was reviewed. Non-compliances observed during the inspection were listed in the full report regarding on-site audit and technical agreements. These were addressed by the manufacturer to an acceptable level.

9. Personnel

The number of personnel appeared adequate to the present activities. The personnel met during the inspection were aware and followed the GMP principles with appropriate qualifications and experience. The key personnel of the various department had pharmaceutical qualifications and were well experienced in pharmaceutical manufacturing. An approved company organisation chart was documented.

10. Training

QA was responsible for training of personnel, newly appointed and job specific training and re-training in the event of personnel errors, resulting in a CAPA event. The company has established a training centre to allow the volume of personnel training. Personnel received induction training upon appointment including training on GMP Principles.

11. Personal hygiene

Personnel hygiene requirements were documented in an SOP. The requirements for entry Grade D cleanrooms were well documented, including pictorial drawings in change rooms. Staff observed in these areas were dressed in appropriate protective clothing.

12. Premises

Track 2 inspected is multi-product not dedicated OSD facility. Manufacturing areas were of a good standard and suitable for the activities conducted therein. Exposed surfaces were smooth, impervious and unbroken to minimize the shedding or accumulation of particles or microorganisms and permitted the repeated application of cleaning. The classified areas were monitored for temperature, relative humidity and pressure differentials for environmental control.

FG storage areas in the Track 2 were visited. Demarcation was provided for the storage of rejected, recalled or returned materials or products.

QC laboratories were separated from production areas. Adequate storage space was provided for samples, reference standards, solvents, reagents and records. Stability chambers and retention samples were placed in secured rooms in different buildings from where the QC labs were located.

13. Equipment

Equipment installed in the production block Track 2 was multi-purpose. Each piece of equipment had a unique identification number. Access control, alarm system and audit trail of a granulation equipment was checked. Equipment cleaning were performed CIP or manually as per SOPs.

Utilities

Adequate ventilation, air filtration and exhaust systems were provided. The HVAC system providing filtered air to the Grade D cleanrooms was visited and found acceptable.

Purified water

Purified water was produced from bore well water. The PW system P & ID was in place. PW system was in ambient temperature and the distribution loop was sanitized regularly. PW sampling, testing and trending for microbial testing results for 2019 were reviewed and found acceptable.

14. Materials Management

Incoming raw materials and finished products manufactured were quarantined after receipt until released for use or distribution. Materials and products were stored under the specified conditions.

Starting materials and packaging materials for FPPs stored in Track 2 warehouse were managed by computerized system. The manual inventory logs were also used.

Raw Material Warehouse

Track 2 warehouse was well designed and the layout acceptable. The warehouse was equipped with sensors for temperature and humidity monitoring. The locations of the sensor were based on a temperature mapping study.

Materials' status of raw material was indicated, with respect to material under quarantine, approved, and retest and re-quarantine. Materials sample for QC testing were adequately labelled. The warehouse was equipped with sampling booths under LAF with separate entrances for materials and personal.

A separate locked and secure area were designated for rejected materials. The register for rejected materials was available for review.

Finished Product Store

A Track 2 FG storage room in Track 2 production area was visited. The relevant records of WHO grade Lamivudine Tablets and product status were checked. The FG storage expansion was under consideration by the company at the time of inspection.

15. Documentation

Documentation was designed, prepared, reviewed and distributed according to a documented procedure. Authorized master formulae were available for Lamivudine tablets. Batch manufacturing records (BMRs) were retained for each batch processed. Manufacturing & packaging batch records of PV batches were reviewed and found acceptable.

An SOP for product batch numbering and an SOP for issuance and control of manufacturing work order, BMR and BPR were reviewed. Some weaknesses were noted. These were addressed in CAPAs by the manufacturer to a satisfactory level.

16. Good practices in production

The manufacturing processes were performed and recorded according to instructions in the batch production records. Production of several tablets other than Lamivudine tablets was in operation at the time of inspection. Tablets manufacturing steps including material dispensing, granulation, compression, coating and primary, secondary packaging and finished product storage rooms in Track 2 were inspected. Manufacturing records of the products under production were spot checked and found acceptable. The material transfers during production are conducted in closed system for products with large batch size. Intermediate materials transferred for product in small batch sizes such as WHO Lamivudine tablets were performed manually.

Punch and die:

The control and management procedure for issuance /return of punch and die was available. A punch and die usage log, release and maintenance records for Lamivudine tablets was checked and found acceptable. The register for the disposal of punches and dies was reviewed. Reason for disposal was documented.

Compression:

A Track 1 tablet product was observed in operation at a compression room of Track 2 at the time of inspection. The management procedure of this kind operation was discussed. The concern was addressed with risk assessment and contract agreement by the company.

Coating:

The coating process for a tablet product was in operation at the time of inspection. The holding time for the coating solutions was specified. In-process control was performed as per procedure.

Tablet inspection:

Tablet inspections were performed by both automated equipment and manual check. The company confirmed that manual tablet inspection was not used for the WHO Lamivudine product. In-process controls were conducted at several IPC laboratories area inside of the Track 2 production block. Appropriate testing equipment is available.

Primary and secondary packaging:

A bottle line for primary and secondary packaging was in operation at the time of inspection. The company had introduced coding and scanning procedures to manage the packaging operation to control/identify the various components of packaging materials and the individual product packs, i.e. serialisation for the products supplied to certain destination market. The procedure and control with documentation for line clearance before commencing the next production was in place.

17. Good practices in quality control

The QC function was independent of other departments. QC laboratories of OSD Track 2 were separated from production areas. It was housed across two floors including microbiological laboratory. The microbiology laboratory was segregated from the chemistry laboratory.

Sample handling and testing:

An access-controlled sample receipt area for samples was available. Sample register and the information for receiving and distribution were checked. The traceability of raw data was available in the sampling records.

The weighing of starting materials was reviewed. The procedures and logbooks, calibrations, daily weight checks temperature and humidity monitoring were in place.

Packaging material testing was checked. A sampling plan for QC testing was available and listed the packing testing.

A procedure for finished product release testing for tablets was reviewed and found acceptable.

Retention samples:

Retention samples were kept in a secured and temperature-controlled room which was in the building separate from the Track 2 QC lab. The retention sample register and samples of each batch finished product produced were kept with double quantity of full testing. Annual check for the sample was performed according to the company procedure.

Stability study:

Stability study chambers were placed in a technical floor and qualified for stability study under different conditions. The stability study registers and samples under condition of 30°C/RH75% were checked. Some discrepancies were noted and were addressed with CAPA by the company to a satisfactory level.

Instrumentation:

The company had adequate quantity of instruments and equipment for QC laboratory activities. The records and logs were adequately maintained. Status labels were attached to equipment and found acceptable. Calibration status and re-calibration dates were acceptable. A balance room equipment was further checked and found to comply with respect to calibration labels and status. Daily weight checks were performed as well as temperature and relative humidity was recorded as per SOP twice daily.

QC chromatographic analysis was operated and control with computerised system. IR instruments link to software server. Access to IR was adequately controlled. The IR analysis of lamivudine spectrum was checked and found acceptable.

Particle size distribution analysis of Lamivudine API for validation batch manufacturing was checked. The data was reviewed and met the specification. The annual calibration, during the last calibration was found acceptable.

Reference standards and substances

Primary reference substance and secondary working reference standards with specified shelf life were stored in a temperature-controlled refrigerator.

Official primary reference substance of lamivudine checked was available. The register for the use of reference standard was maintained.

Solvents, reagents, buffers solutions were adequately labelled with date of preparation and valid up to date included. The grade of volumetric equipment was spot checked and comply with Class A requirements.

Microbiology Laboratory

Microbiological laboratory was adequately equipped and appeared to be of an acceptable standard for non-sterile products. Media preparation and sterilization procedure and records were reviewed. PW testing procedure, records and monitoring results for microbiological limit was spot checked. The monitoring results appeared acceptable.

Part 3	Conclusion – Inspection outcome
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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, **Beximco Pharmaceutical Limited**, located at **Track-2, 126, Kathaldia, Auchpara, Tongi-1711, Gazipur, Bangladesh** 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
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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