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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	Shanghai Harvest Pharmaceutical Co., Ltd.
Corporate address of manufacturer	No. 805, Jinhu Road, Pudong, Shanghai, P. R. China
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Shanghai Harvest Pharmaceutical Co., Ltd. No. 805, Jinhu Road, Pudong, Shanghai, P. R. China
Unit / block / workshop number	Line 5, Line 7, Line 8, Line 9
Inspection details	
Dates of inspection	21 – 24 January 2019
Type of inspection	Routine inspection
Introduction	
Brief description of the manufacturing activities	The main activity of Shanghai Harvest Pharmaceutical Co., Ltd. at the site was the manufacture, packaging, labelling, testing, storage and distribution of small volume parenterals. Only pharmaceutical finished products (FPPs) were manufactured. Since the last WHO inspection, new SVP filling lines 8 and 9 were installed. PW and WFI systems were extended to accommodate the new SVP lines. A new WFI distillation apparatus was installed. A new warehouse for precursor chemicals was established. A new area was dedicated to rejected and returned psychotropics.
General information about the company and site	Shanghai Harvest Pharmaceutical Co., Ltd. (hereinafter referred to as SHP) is a FPP manufacturer located at No. 805, Jinhu Road, Pilot Free Trade Zone, Shanghai, China. SHP was established in November 1993 by 3 parties, Tianfeng Pharmaceutical Factory, a subsidiary of Shanghai Pharmaceutical Co., Ltd., Harvester Trading Co., Taiwan and Elan Pharma, Ireland. The company moved to its current location in 1999. The site is located on 20000m^2 area and includes several buildings. A contract warehouse on 158, Gui Qiao Road was used for storing and sampling ampoules. The product portfolio consists of emergency life-saving pharmaceutical products. There were no Penicillin and other β-lactam products manufactured

	on site. Kanamycin 500mg/2mL was manufactured in Line 5. Kanamycin 1g/4mL was manufactured in Line 7. Ribavirin 100mg/mL was originally manufactured in Line 3 but it was planned to be transferred to Line 8 and Magnesium Sulphate 1mg/2mL was manufactured in Line 9.
History	This was the third WHO inspection with the last being in March 2017. The site had been previously inspected by TGA but the company stopped supplying to Australian market in 2013. The site was regularly inspected by CFDA
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Quality management system Production operations with ar focus on Line 5, Line 7, Line 8 and Line 9 Packaging Operations QC Laboratories and control system Materials management system Facilities management and engineering support systems including HVAC, water etc. Note: Line 3 where existing batches of Ribavirin were manufactured was not operational. Therefore, only a review of documentation was performed in relation to Ribavirin batches that had been manufactured on Line 3
Restrictions	The scope of the inspection was focused on the formulation, filling, terminal sterilisation and packaging of Kanamycin solution for injection. Two pack sizes were manufactured; 0.5g Kanamycin, (2ml in a 3ml ampoule) on production Line 5 and 1 g (4 ml in a 5 ml ampoule) on Line 7 respectively. In addition, Ribavirin for off label use in an emergency treatment of Lassa fever in a clinical trial setting (ERP) was included in the scope as well as Magnesium Sulfate in ampoules which was about to be submitted for prequalification.
Out of scope	The injectable products manufactured on this site included both aseptically manufactured and terminally sterilised parenteral preparations. Products not submitted to WHO for prequalification or ERP purposes were excluded from the scope of this inspection
WHO products covered by the inspection	TB 317Kanamycin Monosulfate (2ml:0.5g) TB 318 Kanamycin Monosulfate (4ml:1g) Ribavirin 100mg/ml (ERP) Magnesium Sulfate 1mg/2ml (to be submitted for prequalification)
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 (where applicable)**

1. Pharmaceutical quality system

A system for quality assurance was established, with procedures covering key quality elements in place. The procedures were reviewed and discussed during the inspection. Operations were specified in written form and GMP requirements were essentially being met. Managerial responsibilities were appropriately specified in written job-descriptions. Product and processes were monitored, and test results taken into account during batch release; regular monitoring and reviews of the quality of pharmaceutical products were being conducted according to documented schedules and procedures. BMRs were reviewed by QA and approved/released by Quality Director or his deputy.

Product quality review

Annual product quality review was performed according to a documented procedure. PQRs had to be completed within 3 months. There was no plan available for prioritizing and monitoring PQRs. 31 batches of Ribavirin were manufactured on Line 3 in 2018. There was no statistical analysis on the yield. Production of Ribavirin was planned to be transferred to Line 8. No PQR for Magnesium Sulfate was performed since only registration batches had been manufactured. The 2016 and 2017 PQRs of Kanamycin 500mg/2mL were reviewed. 28 batches were manufactured in 2016, no batches were manufactured in 2017 and 2018. Identified observations were adequately addressed by the company's CAPA plan

Data integrity management

Policies and procedures were introduced and updated to better assure data and record management systems. However, it was noted that three work stations supporting standalone HPLCs were operating on Windows XP. Entry ports on these work stations were not protected. Two out of three work stations were operating using Empower 2 which was outdated. Identified observations were adequately addressed by the company's CAPA plan.

Change and deviation management

The company had SOPs in place for change and deviation management. The change controls for the extension of PW and WFI loops were reviewed in detail. Deviations were not trended and reviewed periodically and during investigations there was no checking for potential recurrence. CAPA in relation to deviations were documented but their effectiveness was not verified. Identified observations were adequately addressed by the company's CAPA plan.

Quality Risk Management

The company's procedures on "Quality risk management" were reviewed. The change control SOP also included a section on risk assessment of new product introduction.

2. Good manufacturing practices for pharmaceutical products

Good manufacturing practices generally were implemented. Necessary human and physical resources were provided, including qualified and trained personnel, adequate premises, suitable equipment and services, appropriate materials, approved procedures and instructions, for in-process and other controls. Qualification and validation activities were generally being performed. Manufacturing steps were recorded in batch manufacturing and packaging records. Manufacturing processes were defined and reviewed. Product was released by the authorized persons

3. Sanitation and hygiene

Premises and equipment were maintained at a satisfactory level of cleanliness. The company had procedures in place as the basis for its approach to personal hygiene and sanitation in its production facility, with appropriate hand washing required. Clean areas were cleaned frequently in accordance with an approved written programme.

Personnel were seen to be performing their duties in a generally organized and diligent manner. No significant gowning violations were noted during the periods of production observed. Procedures were in place for the preparation and control of sanitizing materials used in production areas.

Non-viable and microbial monitoring of facilities were performed. The risk basis for the sampling plans was discussed with the company and documentation in support of the locations chose for monitoring and qualification to be improved.

4. Qualification and validation

The company approach to validation was in accordance with the Validation Mater Plan. A validation programme was available. In general SHP had identified the qualification and validation work that was required. The revalidation was performed periodically. The key elements of a qualification and validation programme were defined. Documentary evidence was available that the equipment and processes have been designed, installed, operated in accordance with their design specifications.

Requalification of Ampoule Terminal Autoclave was reviewed. Similarly, requalification of the automated optical control machine (Line 5) was reviewed. SHP performed requalification by carrying out the protocol that the manufacturer of the equipment had provided. In addition, Knapp test was performed. Requalification of filling Line 5 as well as requalification of the HVAC system supplying to the filling area. The depyrogenation tunnel of Line 8 was reviewed. Identified observations were adequately addressed by the company's CAPA plan.

Gowning qualification

The SOPs on "Gowning procedure for Clean Areas" and "Gowning qualification for grade B" were reviewed. Gowning re-qualification was performed periodically and monitored with contact plates.

Visual inspector's qualification

The procedures for both automated and "Visual inspection/optical control" and associated operator and QA staff qualification of visual inspection and optical control" were reviewed. This included

checks on the ability to detect dye test failures. SHP applied this test only for Kanamycin. The approach was generally satisfactory.

5. Complaints

There was a procedure in place for complaints handling. Responsibilities were described and an appointed person in QA was responsible for coordinating complaint handling. Complaints were not reviewed periodically and there was no provision to check for recurrence during root cause investigations. Complaints were closed out one month after replying to the complainant, if no further response was received. No complaints for Ribavirin were registered for the last 5 years (no batches were manufactured in 2016). Identified observations were adequately addressed by the company's CAPA plan.

6. Product recalls

A procedure for handling recalls was presented but it did not include details on handling recalls of products distributed outside of P.R. China. The Quality Director was responsible for managing the recall of a product. A mock recall was required to be performed annually unless a recall had taken place. In 2017 and 2018 no mock recall was carried out since a product was recalled at the end of 2017 and the recall process was completed in 2018. Records of the recall were made available and were reviewed during the inspection.

7. Contract production, analysis and other activities

Production and quality control operations for Kanamycin injection were not contracted out. The testing method was in-house and different to the method described in the USP monograph. Testing of Kanamycin API was contracted to Shanghai Institute for Food and Drug Control. A contract was in place.

HEPA testing and autoclave temperature mapping was contracted out and agreements were in place.

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

Self-inspection was not covered in detail by this inspection. There was a procedure in place for supplier approval, evaluation and requalification. Two suppliers of Ribavirin API were registered and spot checks on the records for approval and requalification were made. Similarly records for one of the ampoules suppliers were reviewed and were found adequate. Documentation regarding the approval of the Magnesium Sulfate API supplier was made available.

Testing of Kanamycin API was contracted to Shanghai Institute for Food and Drug Control. The contact was signed in May 2017. Since this was a state laboratory, it had not been audited but the contract included a clause that allowed SHP to audit the laboratory, when necessary.

9. Personnel

There were approximately 250 staff working on site, at the time of inspection. In general, personnel had the necessary qualifications and practical experience. Responsibilities of staff, and their duties were documented in written job descriptions. The job description of Quality Director was reviewed during the inspection. Personnel interviewed during the inspection were aware of the principles of GMP. An organization chart was available and was considered acceptable.

All personnel were required to undergo an initial health examination prior to and annually during employment. Personnel conducting visual inspections had to undergo periodic eye examinations. However, the relevant procedure did not detail the exclusion of non-qualified personnel because of failure in eye examination tests. Identified observations were adequately addressed by the company's CAPA plan.

10. Training

There were several training procedures in place dedicated to specific posts. Training evaluation criteria were established but they were extremely strict which could lead to inappropriate disqualification of personnel. Training was spot checked for operators performing visual inspection.

11. Personal hygiene

Smoking, eating, drinking, chewing, and keeping smoking material and personal medicines were prohibited in production, laboratory and storage areas. However, there was no requirement to report and document persons that were excluded from production areas because of medical reasons. Identified observations were adequately addressed by the company's CAPA plan.

12. Premises

Generally, premises were located, designed, constructed and maintained to suit the operations to be carried out. Some discrepancies were noted in personnel change rooms. The same entry was used for personnel and visitors to production facilities, but different rules applied to gowning rooms for visitors and staff. The layout and design of premises was such as to minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination. Premises were designed and constructed to facilitate good sanitation. Identified observations were adequately addressed by the company's CAPA plan.

Apart from the warehouses located on site, there was a contract warehouse located on 158, Road Gui Qiao where ampoules were sampled and stored. The construction of core filling and operation area of production facilities was designed with Grade A air supply with Grade B background, followed by terminal sterilization autoclave. Exposed surfaces were smooth, impermeable and unbroken to minimize the shedding or accumulation of particles or microorganisms and permitted the repeated application of cleaning agents and disinfectants, where necessary. Critical airlock doors could not be opened simultaneously. A pest control programme was established, and it was managed by HR department

13. Equipment

The equipment installed for Line 5 (3rd floor) and Line 7 (4th floor) was of an acceptable standard. Similarly, two new Lines (8 and 9) were installed on the 4th floor and were operational. The facility and equipment appeared to be running well with no significant interruptions. The detailed procedures for the operation of key equipment were generally well documented. All fixed pipework was labelled to indicate the contents and the direction of flow. However, it was noted that some equipment and tools did not bear identification codes. Line 3 where existing batches of Ribavirin were manufactured was not operational. Therefore, only a review of documentation was performed in relation to Ribavirin batches that had been manufactured on Line 3.

A new distillation apparatus was installed and the PW and WFI loops were extended to serve the newly installed Lines 8 and 9. Spot checks on the maintenance and calibration of critical equipment such as sterilizers, filtration systems, air vent and gas filters were performed and were generally found acceptable. The extension of the PW and WFI loops were reviewed in detail. Identified observations were adequately addressed by the company's CAPA plan.

14. Materials

Incoming materials and finished products were quarantined after receipt until they were released for use or distribution. Quantities of received raw and packaging material were not checked against the placed order and there was no provision to check vehicle cleanliness and transport conditions upon receipt of raw materials. Temperature at the warehouse was maintained between 10-30°C which was not appropriate for all APIs (e.g. Furosemide). Identified observations were adequately addressed by the company's CAPA plan.

Starting materials and packaging materials were purchased from approved suppliers. The company used the principle of fi-fo for management of materials.

Rejected, returned, recovered, reprocessed and reworked materials

Rejected materials and products were marked as such and stored separately. A new area was dedicated to rejected and returned psychotropics.

15. Documentation

In general documents were designed and prepared, reviewed and distributed with care in general. However, some documents did not carry the item codes referred to, and the use of item codes was not consistent in the batch paperwork.

Batch manufacturing records (BMRs) were retained for each batch processed. Kanamycin injection BMRs were reviewed and it was observed that the design of the batch record did not facilitate recording of all necessary information at the time it happened. Similarly, BMRs of Ribavirin manufactured in Line 3 were reviewed. Identified observations were adequately addressed by the company's CAPA plan

16. Good practices in production

Commercial batches of Kanamycin were produced in 2016, no batches were manufactured after 2016. The product was still pending WHO prequalification. Ribavirin was manufactured in Line 3. 31batches were manufactured in 2018. Process validation was carried out in 2014 using Line 3. Two approved batch sizes existed. The company had decided to stop production in Line 3 and transfer the product to Line 8 resulting in a change on batch size. Process validation had not been carried out at the time of inspection. Magnesium Sulfate was planned to be manufactured on Line 9. SHP was in the process of compiling a dossier for prequalification. Registration batches were manufactured in December 2018. A study was in progress to assess potential interaction between the injection solution and the ampoule glass.

Manufacture of Sterile preparations

Clean areas for the manufacture of sterile products were classified according to the required characteristics of the environment. Clean rooms and clean-air devices were routinely monitored while in operation. PW and WFI monitoring were performed.

Finishing of sterile products

Filled ampules were inspected individually after terminal sterilization. Inspection was carried out by appropriately qualified personnel or by automated inspection equipment.

17. Good practices in quality control

The QC function was independent from other departments. Adequate resources were available to ensure QC arrangements were effectively and reliably carried out. Chemical and microbiological laboratories were separated from production areas. The Microbiology Laboratory was segregated from the Chemical Laboratory. Sufficient space was given to avoid mix ups and cross-contamination. Adequate storage space was provided for samples, reference standards, solvents, reagents and records.

Stability Testing

A written programme for stability study was available. Stability and on-going stability studies were reviewed. Results between different studies for the same product were not compared. Identified observations were adequately addressed by the company's CAPA plan.

Environmental monitoring of clean area (EM)

The SOP for environmental monitoring in production areas was reviewed and discussed. Contact plates, air samples and settle plates were used for EM.

The report of EM for the last 6 months was reviewed. Local flora isolates were not identified and used during the media fill to confirm growth in the media fertility testing. Identified observations were adequately addressed by the company's CAPA plan.

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, ***Shanghai Harvest Pharmaceutical Co., Ltd.*** located at ***No. 805, Jinhu Road, Pudong, Shanghai, P.R. China*** 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 artemisin is used as a starting material in the production of antimalarial active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 6
Short name: WHO TRS No. 992, Annex 6
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

21. Guidance on good data and record management practices. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5
Short name: WHO GDRMP or ***WHO TRS No. 996, Annex 5***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf

22. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10
Short name: WHO TRS No. 996, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

23. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 10.
Short name: WHO TRS No. 1010, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf