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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	China Resources Zizhu (CRZ) Pharmaceutical Co. Ltd,
Corporate address of manufacturer	No 27 Chaoyang North Road, Chaoyang District, Beijing, 100024, China
Inspected site	
Name & address of inspected manufacturing site if different from that given above	No 27 Chaoyang North Road, Chaoyang District, Beijing, 100024, China
Unit / block / workshop number	W-F-E workshop
Inspection details	
Dates of inspection	22-26 October 2018
Type of inspection	Routine GMP inspection
Introduction	
Brief description of the manufacturing activities	China Resources Zizhu was established in 1969. The site in Beijing is for the finished pharmaceutical products. With a coverage of 122,000 m^2, a floor area of 60,000 m^2 and a greening rate of 45%. Key buildings on the site include the Building for General Pharmaceutical Preparations, the W-F-E Workshop, the Microecologics Building, Warehouses, QC labs and the Power Station.
General information about the company and site	The dosage forms authorized by China Food and Drug Administration (former name) include tablets, hard capsules, small volume injections, membrane, eye drops, extraction of traditional Chinese Medicine and therapeutic biological products (Bacillus subtilis capsules, live), patches, etc.
History	The manufacturing site has been regularly inspected by WHO-PQT.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	**Document reviewed including but not limited to:** • Organization Chart • Job descriptions for key personnel • Personnel training and hygiene • Product Quality Review

	• Quality Risk Management • Responsibilities of the quality units and production • Complaints and Recalls • Deviation control and change control • CAPA procedure • OOS and investigation • Material release • Self-inspection and vendor qualification • Validation and qualification • Equipment calibration • Data integrity • Sampling and testing of materials • Batch processing records • Materials management system • Purified water system • HVAC system **Physical locations inspected, but not limited to:** • **Workshop W-F-E (Production for WHO PQ products)** • W-F-E warehouse • QC laboratories including chemical and microbiological • Retain samples storage • Stability chambers area
Restrictions	None
Out of scope	Workshops that were not used for WHO PQ products were not inspected. This included: - Workshop-1 (nonhormonal and OSD) - Workshop-2 (API work now transferred to QZP) - Workshop-3 (hormone OSD) - Workshop-4 (nonhormonal injectable)
WHO products covered by the inspection	Mifepristone 200mg tablets (RH052) Misoprostol 200mcg tablets (RH048)
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

The quality management system was established according to WHO cGMP, ICH Q10 and Chinese GMP (2010 edition). The General Manager is responsible for establishing quality management system, providing resources required, rational planning, organizing and coordinating to ensure that the quality department can independently fulfill its responsibilities to realize the company's quality policy. The Quality Director, also as Manager of Technology and Quality Department, who is the Qualified Person, is responsible for implementing the company's quality policy, ensuring that all quality-related activities are in compliance with applicable national and international regulatory and technical requirements, supervising the quality management system and ensuring its effective operation. Management Review meetings were held monthly in accordance with an approved procedure.

Quality assurance (QA) was responsible for compiling all data, information and organization as well as minutes of the meetings. Procedures that were reviewed and discussed during the inspection were generally presented promptly.

The Management Review procedure described procedures for management reviews and the Management procedure for quality system review for quality system reviews. The SOPs were reviewed and found acceptable.

Product quality reviews were performed according to the procedure. PQRs were conducted annually on a rolling basis and QA was responsible for approving the reports and monitoring the process which had to be completed within three calendar months from end of product review period.

The QRM procedure was discussed. The procedure covered the entire product lifecycle. The procedure applied to deviations, change controls, complaints, adverse trending identified by PQR, observations identified through self-inspection and more. The risk analysis was performed using various tools such as FMEA, control charts, fish-bone diagram, checklist, and decision tree.

Change control procedure was reviewed. The last update of the SOP was made on the 1st of November 2017 to increase the number of the different categories of changes from two (minor, major) to three (minor, medium, major). The SOP covers all necessary aspects for change control procedure including description of responsibilities, evaluation of product impact and a flow chart for handling changes. According to the SOP classification and evaluation of changes were done by the QP, who also had a possibility to delegate the duty to the QA supervisor. An evaluation team to assess the change was nominated, if needed. After the last WHO inspection ,33 changes in total were managed in the year 2016, 33 in total in 2017, and 21 in total in the year 2018 until the time of the inspection. Company had listed the major changes (4 major / 2016, 5 major 5/ 2017 and 2 major /2018) after the last WHO inspection in the preliminary documentation provided to the inspectors.

Deviation Management Procedures was reviewed and the content of the SOP was found acceptable. 8 deviations had been recorded and handled in the year 2016, 8 deviations in the year 2017 and 10 in the year 2018 at the time of inspection. Several deviations were raised because of problems in stability testing chambers. Handling of the reviewed deviations had been performed following the procedures in an acceptable way.

CAPA management was reviewed and it was found acceptable. During the last three years, 11 CAPA managements had been done. CAPAs may be raised based on e.g. findings from self-inspections, as a part of OOS handling or in the case of repeated deviations (3 similar incidents in 3 months or 10 in 1 year). No extended CAPA managements had been implemented for the products in the scope of the inspection after the last inspection.

Out of specification (OOS) and out of trending (OOT) procedure was discussed. The investigation was done using three phases. Hypothesis will be performed to discount any error from the laboratory. If no root cause was found from the laboratory, Phase II will be initiated. Retesting will be performed including retesting of approved batches and resampling. The procedure did not specify number of retest that should be performed as part of retesting.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

2. Good manufacturing practices for pharmaceutical products

Basic principles of good manufacturing practices were generally described and implemented. Manufacturing processes were adequately defined and documented in BMRs and BPRs. Required resources were available, including adequate premises, equipment and utilities. Appropriately qualified personnel were employed. Similarly, to the previous WHO inspection all areas visited were generally clean, tidy and well-maintained.

3. Sanitation and hygiene

Premises and equipment were generally cleaned according to established procedures according to available SOP's. Change rooms were well maintained and authorized instructions displayed the steps and dress code. Cleaning records of manufacturing rooms and equipment were in place. Spot checks on rodent traps and insecticutors were made. Human resources were responsible for monitoring and controlling the third party providing pest control services.

4. Qualification and validation

The key principles of qualification and validation program were defined and documented in the Validation Master Plan. The VMP of the site addressed validation/qualification activities including but not limited to equipment, utilities, processes and cleaning, analytical methodology, vendors and computerized systems.

5. Complaints

Complaints Management Procedure was reviewed, and its content was found to be acceptable. There were six complaints in 2016, six in 2017, and one 2018 for all products manufactured on this site. None of them did concern Misoprostol or Mifepristone.

6. Product recalls

Product Recall Procedure was reviewed. The content of the SOP was acceptable. Mock recalls had been done in 2013 (export products for commercial channels), 2015 (OTC products domestic market) and 2017 (prescription drugs for domestic market). No mock recall had been performed for products distributed via UNFPA.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

7. Contract production, analysis and other activities

Particle size distribution of Mifepristone API was performed by a contract laboratory Testing Laboratory of China National Academy of Nanotechnology & Engineering, that was ISO 17025 accredited by CNAS (Chinese National Accreditation Service. Testing Laboratory had been audited by CRZ (on-site audit 16.8.2016 and a desk-based- audit 9.4.2018).

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

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

Self-inspection procedure was reviewed. The content of the SOP was acceptable. Annual self-inspection plan for the year 2018 was reviewed, and it was found to cover well all activities. Plan was told to be prepared risk based e.g. taking in account detected deviations, although there was no formal tool for this planning. Data integrity was included as one component in the items to be inspected. Fulfilment of the plan was followed and documented by marking the status of planned self-inspections after they had been performed.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

9. Personnel

In general personnel met during the inspection appeared aware of the basic principles of GMP. Job descriptions of the Head of Quality (QA) and Senior Manager of Quality Control were reviewed and in place. The total number of employees in the whole site involved in QA, QC, production, equipment support, storage and distribution accounts to 336. The number and qualifications of workers was adequate as compared to the activities performed. A general impression from the discussions and when following operators to perform actual work and demonstrations given in the

laboratory was that the employees were well aware of their duties and responsibilities and were technically skillful.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

10. Training

Management procedure for employee training and Management Procedure for Company GMP training described the initial training and the continuous GMP-training training system of personnel. Content of the SOPs was acceptable. According to the SOP initial training and on-site training were given, and the effectivity of training was evaluated in a test (if a person fails two times in the test, he/she was considered not to be able to perform that duty).

Training records and job descriptions of three warehouse operators were reviewed as examples. Content of the job descriptions for all three operators was the same, and they had individually signed the job descriptions. According to their training records, training had been provided to them annually to make sure that they stay trained also in duties that they do not necessarily perform regularly.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

11. Personal hygiene

Personnel gowning procedure was appropriate and was generally followed. Instructions and pictorials to be followed were sufficiently clear when it came to personal hygiene. For new personnel including contract personnel, medical examinations were foreseen before joining the company and yearly afterwards spot checks on medical records of personnel were performed.

12. Premises

Premises were comprised of the following workshops:

- Workshop-1 (nonhormonal and OSD)
- Workshop-2 (API work now transferred to QZP)
- Workshop-3 (hormone OSD)
- Workshop-4 (nonhormonal injectable)
- WFE built in 2012 (independent building, WFE stand for WHO/FDA/EU)
- Workshop 1 and 3 renamed as Workshop-3 but physically separated

Storage areas for warehousing of raw materials and finished product were of sufficient capacity. Temperature and humidity were monitored. Receiving and dispatch bays were separated and were protected from weather conditions.

The air handling units (AHUs) were equipped with double G4 and F8 filters before connected with terminal HEPA (H13) filters. The temperature (18-26ºC) and humidity (45-60%) was maintained and monitored through building management system. Differential pressure was monitored across filters (upstream and downstream) using calibrated magnehelic gauges. The G4 and F8 filters are replaced once every 2 months or if pressure doubled initial pressure. There was no cleaning performed to these G4 and F8 filters hence there was no clean area provided for the cleaning of these filters. It was indicated that AHUs were switched off when these filters were replaced, and this activity was completed within 40 minutes. The replacement was performed after 5pm or after the production activities. The leaks from AHU chambers were performed once every month whereas ducts were not routinely verified except as part of annual preventive maintenance plan. The service / utility area was found to be clean, tidy and well maintained.

The building management system (BMS) office was equipped with few monitors wherein HVAC/PW operator was responsible to record temperature, humidity and differential pressure from these monitors. The BMS office was manned 24 hours. Audio-visual alarm was provided next to the monitor. It was however noted that an alarm logbook was not maintained hence alarms were not recorded. Privileges to change temperature, humidity and differential pressure parameters were with the Senior Equipment Engineer who was claimed to be not part of the WFE workshop. The HVAC-PW operator did not have any privileges to change settings / parameters.

The purified water system was briefly inspected. There were 3 sampling points from the generation system whereas a total of 17 user points for the distribution system. The purified water system was well maintained. The potable water is the source water for purified water which has a capacity to produce 1500L/hour. The potable water passed through multimedia filter, softener, 5µm filter, reverse osmosis, EDI before stored in the purified water storage tank (4000L). Sampling was performed from supply, return and after EDI points.

The purified water treatment plant had three sampling points including supply, return and after EDI tested once/week. There were 17 user points in WFE workshop, each user point sampled and tested for complete testing once / month. Trending analysis of water results are performed once every three months and annually. Quarterly report of April-June 2018 was discussed, the review included TOC, conductivity, microbial limit test for three sampling points and all user points. In general, results of all these tests were well within alert limits.

Warehouse W-F-E, which was dedicated only for materials used in manufacturing in the W-F-E Workshop, was visited on day 2. The warehouse was in good condition and order. Three warehouse operators and a warehouse supervisor were responsible of warehouse operations. It was indicated by the warehouse manager that the received materials were immediately moved from the receiving area (208) to the staging guarantee area (room 203) where humidity and temperature were monitored by a stand-alone-meter. In the large temperature-controlled warehouse room (201) environmental monitoring was done by BMS. Status of materials was indicated by a color code. In the warehouse office there was a computer used to create the labels. A common password for all warehouse personnel was used to log in to this computer that is not acceptable. A calculating error was noticed on the inventory card of material A0019200004104 (microcrystalline cellulose). Inventory balance

was marked to be 194,822 kg, even when one full 20 kg bag and some amount of another bag had already been taken to production out of 200 kg total amount.

The QC laboratory was located in the technology building alongside meeting rooms and office rooms. Laboratory activities were performed on two floors, sample receiving, microbiological laboratory, stability chambers, weighing room, storages for reagents and standards and wet chemistry in the 3nd floor and the instrumental laboratory in the 2nd floor. Retain samples were stored in the 1st floor. Laboratory areas were visited on days 3, 4 and 5. QC laboratories were in general in good order and spacious enough to separate clearly different activities and allow adequate working space. Organization of the laboratory was not always logical, e.g. control bacterial strains were stored in the same room as media, which brings a risk of contamination and another of the microbial limits testing rooms had two work stations, but it was told that only one is used at a time. The QC area was older than the W-F-E warehouse and production areas.

Copies of necessary SOPs, log books and manuals were stored near the corresponding equipment and instruments and were easily found during laboratory visits.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

13. Equipment

In general, equipment was appropriate for the manufacture of OSDs. Records for calibration, qualification and maintenance were available.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

14. Materials

There was a procedure in place describing receipt and storage of raw materials. A check list was used for receipt of raw materials. Temperature and relative humidity were monitored and controlled.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections

15. Documentation

A documentation system was in place. Procedures defined and supported manufacturing and quality control operations. In general documents were approved, signed and dated by appropriate responsible persons, reviewed and kept up to date. Specifications and testing procedures were available. In the QC laboratory it was told that a dedicated person was responsible for ensuring that copies of instructions are available at the work stations and kept up to date. Copies of expired versions are removed and destroyed. No expired versions were found during spot-checks.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

16. Good practices in production

The layout of the WFE workshop was reviewed. A separate WFE warehouse was maintained for all incoming materials such as actives, excipients and packaging materials related to WFE workshop (production of WHO PQ products). A separate pallet warehouse was maintained for non-WFE products. The WFE warehouse was exclusively used for storing and sampling excipients and primary packaging materials. Based on the production schedule, APIs were transferred to WFE workshop for sampling and dispensing. Sampling and dispensing of APIs were performed inside the WFE workshop. The dispensing was performed by the production personnel and claimed to be verified by the warehouse personnel.

The inspector visited the WFE workshop (production) in the afternoon of day 2. The workshop was found clean, tidy and well maintained as noted. At the time of inspection, production activities were not in operation. Areas inspected included sampling booths, dispensing areas, granulation, compression rooms, and primary packaging areas.

Most of the production operations were carried out in closed systems. The APIs and excipients were dispensed and transferred to in-process bulk containers (IBCs) using the isolator. Misoprostol 200mcg tablets was produced using direct compression method whereas Mifepristone 200mg tablets was produced using a wet granulation method. The company has not supplied any batches of Mifepristone 200mg tablets to UNFPA.

The compression machine (IMA) was used for the compression of Misoprostol 200mcg tablets. With the use of lifting and positioning device, IBC was loaded as a hopper to the compression machine. A single rotary 45 station machine was used which was equipped with a metal detector and de-duster. The bulk tablets were blister packed using an automatic packing line. The blister packing machine was equipped with a camera system.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

17. Good practices in quality control

The laboratory is located in the Technology building spread over three floors as follows:

- 1st floor for sample retention and temporary storage area for samples waiting to be moved to stability studies
- 2nd floor for instrumentation section (HPLC/GC) and one dissolution test equipment
- 3rd floor for sample receiving, microbiology laboratory (two microbiological limit testing rooms, incubator room, refrigerator room (for storage of media and microbial strains), sterility testing area (not in the scope of this inspection), autoclaves for media and to destroy cultures), wet chemistry laboratory (IR/UV, storage for reagents, storage for standards, weighing room), water treatment for laboratory use and stability section (7 stability chambers)

Quality control laboratories were separated from production areas. Chemical laboratories as well as the microbiological laboratory were visited. The QC laboratory was well organized and equipped. Analytical equipment was installed in separate rooms and logbooks for use and maintenance of equipment were presented. Empower 3 software was used to network GC and HPLC equipment. Different roles and access rights were established. Practices in the Microbiological laboratory were also reviewed. Procedures and records for preparation of culture media, growth promotion and consumption of materials and reagents were spot-checked.

The laboratory and QA staff accessed the laboratory using an access card. Samples were collected by the QA and sent to the laboratory along with test request slip containing the name of the product, Batch No, quantity, material code and full or partial testing. A separate sample inventory logbook for in-process and finished product was maintained by the laboratory. It was noted that samples received from the WFE workshop (meant for export market) are taken after the primary packaging operations i.e. blister packaging whereas for domestic markets, bulk tablets were sampled for chemical / physical testing and blisters for microbiology testing. It was indicated that group leaders of various sections maintained the competency matrix of their analysts before assigning samples for analysis.

Specifications of both products and APIs were provided to the inspectors.

Retention samples

The storage area for retention samples in the 1st floor was visited on day 4. The area was generally in good order. Temperature and humidity were monitored properly by stand-alone meters and data loggers. It was noticed, however that samples that had been taken for stability studies were stored in the area for retention samples without indicating which locations are dedicated for those samples, which could cause a risk of mix-ups.

Stability studies

Stability chambers room located in the 3rd floor was visited on day 4. Several abnormalities had been recorded as deviations in the functions of stability chambers. A formal CAPA investigation had not been raised, but instead of that deviations had been handled as individual incidents, because there was no common root-causes identified in them. According to the CRZ personnel, it had been possible to solve the problems with the help from the manufacturer of the chambers, and recently there had been no incidents.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall 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, ***China Resources Zizhu (CRZ) Pharmaceutical Co. Ltd***located at ***No. 27 Chaoyang North Road, Chaoyang District, Beijing, 100024, 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