World Health Organization

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Prequalification Team Inspection Services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Active Pharmaceutical Ingredient Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**CR SanJiu (Youyang) Pharmaceutical Co., Ltd (formerly KPC Chongqing Wuling)**
Corporate address of manufacturer	108, Southern Jinyuan Road, Banxi Light Industry Area, Youyang City, Chongqing, China
Name & address of inspected manufacturing site if different from that given above	CR Sanjiu (Youyang) Pharmaceutical Co., Ltd 108, Southern Jinyuan Road, Banxi Light Industry Area, Youyang City, Chongqing, China
Synthetic unit /Block/ Workshop	Building 1, Artemisinin extraction Building 2, production of Dihydroartemisinin (DHA)
Inspection details	
Dates of inspection	22-26 April 2024 18-21 March 2025
Type of inspection	Routine GMP inspection
Introduction	
Brief description of the manufacturing activities	The manufacturing site was initially built in Zhongduo, a town in Youyang. It gained a Chinese GMP certificate and was accepted by WHO inspection for compliance with WHO GMP in 2005, 2010, 2015, and 2018. The site is also qualified to supply multinational pharmaceutical companies and other foreign customers.
General information about the company and site	CR Sanjiu (Youyang) Pharmaceutical Co., Ltd (hereafter "Youyang Pharmaceutical") is located in Youyang County, Chongqing, China. It was established in 1986 and acquired by Holley Group in 2000. It has been a subsidiary of KPC Pharmaceuticals, Inc. since 2017. The company specializes in the production of artemisinin and derivative APIs
History	The old manufacturing plant was located in Zhongduo County, Youyang City, Chongqing, China (about 15km from the existing site) and was inspected by WHO PQ in 2005 and 2010. The existing new plant was inspected in 2014, 2018, April 2024, and March 2025.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	The following activities were undertaken during the inspection: 1. Quality management 2. Personnel and training 3. Premises and equipment 4. Complaints and recalls 5. On-site verification of the evidence of CAPAs 6. Quality control, and microbiology laboratory

	7. Manufacturing areas covering Artemisinin (synthesis) and DHA (powder processing areas)
Restrictions	None
Out of scope	The manufacture of intermediates, APIs, and finished products (TCM) other than Dihydroartemisinin (DHA) was out of the scope of this inspection.
WHO APIs covered by the inspection	Dihydroartemisinin/DHA (WHO API-239)
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original, and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
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
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
KF	Karl Fisher
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
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
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer

Part 2	**Summary of the findings and comments**

1. Quality management

The site had a formal, documented quality system that met most of the current WHO GMP Guidelines requirements. The QA and production departments were independent of each other and reported to the General Manager. The site procedures reviewed and discussed during the inspection were generally satisfactory. Products and processes were monitored, and results were considered during batch release. The entire quality management system was manually managed, as no electronic system was used.

Product quality review (PQR)

The SOP for annual product quality review was reviewed, which was available in Chinese and English. The SOP provided the purpose, scope, responsibilities, definition, and procedures. The PQR was prepared for January-December every year. The procedure stated that a quality review would still be performed if the product was not manufactured during the review period but was in circulation on the market. In general, the contents of the annual review were adequately identified. In addition to performing trend analysis, the process capability index (CpK) as per 6-sigma was also calculated. The CpK assessment criteria were established in the procedure and calculated using Minitab. The quality manager approved the PQR and shared a copy with the production manager. In general, the procedure appeared adequate.

Quality risk management (QRM)

The SOP on QRM was reviewed, and it was noted that the principles of QRM were implemented throughout the product lifecycle, from the introduction of new products to the end of the product lifecycle. Broadly, risk analysis was divided into prospective and retrospective risk analysis. The procedure described various tools required for conducting risk analysis. The procedure was referenced to ICH Q9, providing appendices such as the QRM flow chart, risk register, report, and QRM plan template. In general, the procedure appeared adequate.

Data integrity (DI)
The data management procedure was reviewed, and it was noted that the procedure described ALCOA+ terms. In addition, another SOP, Good Recording Practices, guides the completion of records, including date/time formats, data printouts, corrections to data, handling damaged records, and other related matters. The quality manual provided a high-level statement about data integrity requirements. Additionally, the DI policy, signed by the General Manager, was based on references from CFDA, USFDA, WHO, and MHRA. Based on this high-level policy document, the company performed a data integrity assessment report covering equipment and instruments used in the laboratory, warehouse, and other areas.

Nitrosamine risk assessment
Management of nitrosamine impurities control provided a procedure for managing nitrosamine impurities. In addition, the nitrosamine risk assessment of micronized DHA was reviewed, which provided a comprehensive overview of the manufacturing process, including the potential sources of nitrosamines (raw materials, solvents, reagents, purified water, production equipment, and recovered solvents). The RPN was used to calculate risk, and no risk was identified. A separate nitrosamine risk assessment was performed for Artemisinin, covering Alkyl Azoxy and Aflatoxin content. It was concluded that there was no risk of nitrosamines in DHA. It was noted that solvents were recovered from Artemisinin inside the production area, whereas for DHA, no solvent recovery was carried out.

Elemental impurity risk assessment
The elemental impurity risk assessment was performed per the ICH Q3D requirements.

Batch release
The company had a procedure for the batch release of finished products. The procedure adequately defined the process for releasing intermediates and finished products. The QA released all products. The register for the release of Crude DHA (annex to the SOP), the annex to the SOP, and refined DHA were presented. The release process did not raise any comments.

Deviations
A procedure for deviation management was in place. In 2023, two deviations were reported, and no deviations were reported for 2024. Meanwhile, 33 batches of refined DHA were manufactured in 2023, and 7 batches were manufactured in 2024 up to the inspection date. The training record associated with the training on the SOP for deviation handling was presented.

Self-inspection
The SOP “GMP audit” was available. The selection, training, and qualification of internal auditors were developed. The self-inspection plans for 2024 and 2023 were available. The topics to be covered were QA, QC, Supply management, Sales department, Production support, Artemisinin extraction workshop, finished product department 1 (syrup), and finished product department 2 (DHA, artesunate, artemether). The report for finished product departments 1 & 2 was presented. The self-inspection was performed. In total, six auditors stayed together during the self-inspection from 08:00 to 15:00, with a lunch break of approximately one hour. A checklist was available. 10 deficiencies were found. The self-inspection process was deemed acceptable.

CAPA management

The SOP for "Corrective and preventive actions" (CAPA) was available. The SOP adequately described the methodology to ensure that deviations (production, QC), deficiencies, complaints, observations raised during audits, or identified potential risks do not occur, and how to reduce incidents or serious issues. The different steps were as follows: 1: Investigation of the root cause or non-conformity; 2: Proposal of initial corrective or preventive action; 3: Confirmation of the implementation of the CAPA to ensure that it was completed on time and effectively following the approved content; 3: Tracking of the implementation of the CAPA; Evaluation of the adequacy of the CAPA; Regular review of the CAPA.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

2. Personnel

Approximately 177 employees were working at the site. Production operated either on 12-hour shifts (for Artemisinin extraction and refining of the Crude DHA) and the refining of Crude DHA) or on one-shift production of the Crude DHA. 90 employees were dedicated to the production department and 25 to the quality department. It was declared that the staff in production and QC were permanent staff, and no externally contracted temporary workers were employed. The organigram of the site was presented. A document related to occupational health management was presented. It was declared that operators working in the manufacturing workshops who were exposed to solvents were required to undergo specific medical examinations.

Training

The SOP "Training management" was available. The annual master training plans for 2023 & 2024 were also available.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

3. Buildings and facilities

The manufacturing site is located on an area of 207956m^2, with 32,996 m^2 of construction. The site is composed of five (5) buildings for productions (Building 1, 2, 3, 4, and 5) dedicated respectively to manufacturing artemisinin and its derivatives, Nicotine (Starting Material), Chinese traditional herbal medicine, and Syrup. There are six (6) warehouses in total. Warehouse No. 1 stores raw materials, excipients, intermediates, and finished products. No. 2 is used for storing Artemisia leaves, raw materials, intermediates, and finished products, and No. 3 is specified for Nicotine; there are two (2) solvent tank farms and one (1) chemical material warehouse. One (1) office building is located in the Quality Control area, and the other buildings are for support.

Crude artemisinin was manufactured on the second and third floors of Building 1. Seven operations were carried out here: extraction, separation, concentration, crystallization, crystal washing, drying, and packaging. Artemisinin's clean area (Class D) was located on the first floor of Building 1, covering an area of approximately 410 m². Dissolution, precipitation, filtration, concentration & re-crystallization, drying, and primary packing are carried out here.

Building 2 is a two-story building with a total area of 2,350 m², designed to produce Artemisinin derivatives, specifically Dihydroartemisinin (DHA), Artemether, and Artesunate. Synthesis areas, equipment, and purification cleanrooms, equipped with specified HVAC, are dedicated to each product. The facilities are subdivided into five (5) areas:

1. Floor 1: Artemether synthesis area and cleanrooms for purification, HVAC, and Purified Water.
2. Floor 2: Dihydroartemisinin synthesis area and cleanrooms for purification, HVAC; Artesunate synthesis area and cleanrooms for purification, HVAC.

Dihydroartemisinin was manufactured on the second floor of Building 2, utilizing a clean area (Class D) of approximately 240 m² for purification. Seven operations were carried out here: reaction, separation, crystallization, and drying for the crude product, as well as recrystallization, drying, and mixing for primary packing of the final product.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

4. Process equipment

The manufacturing area was equipped with equipment such as extraction tanks, synthesis tanks, separation tanks, separation columns, crystallization tanks, centrifuges, dryers, and blenders. The construction material for this equipment was confirmed to be SS 304. In addition, the quality control laboratory was also equipped with several equipment and instruments.

The SOP “Maintenance plan for equipment and facilities” was available, which contains the main principles of equipment and facility maintenance. The SOP “Management of metrological appliances” was available. The calibration schedule for the measuring devices was presented. The company hired the services of 2 third-party companies for the calibration of the measuring devices:

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

5. Documentation and records

The batch manufacturing record issuance logbook was reviewed. It included the name of the product, code number, API or intermediate, and master batch record code number. The batch manufacturing and packaging record of crude DHA was reviewed. Two batches of Artemisinin, along with Sodium Hydrogen Bromide, Glacial Acetic Acid, and methanol, were taken to produce the pure DHA. The list of materials, containing quantities issued by the warehouse to production, was available. It was noted that the warehouse did not dispense the actual quantity; instead, it issued one pack. The production

dispensed the quantity of the input materials, and an additional quantity was returned to the warehouse. The cleaning status of all four reactors was available in the batch record.

The specification for micronized DHA was reviewed and compared against the specification submitted in the open part of the DMF. The tests listed in both documents were comparable. The specifications for non-micronized DHA were compared with those provided in the open part of the DMF and found to be equivalent. The specification for crude DHA was reviewed. The specification for Artemisinin was verified and found comparable to the one submitted in the DMF. The specifications and testing procedures were not available in English.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

6. Materials management

The SOP for supplier management was discussed. Based on the risk assessment, the materials were classified into A, B, and C levels, where Class A materials pose the highest risk, affecting the quality of the drug, Class B poses a moderate risk, and Class C poses a low risk. The suppliers were qualified before receiving supplies from them. The supply department requested a list of documents for an initial assessment before samples were tested and used for a trial batch. The material was qualified based on this assessment. The company then performed an on-site audit.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

7. Production and in-process controls

The inspector visited Building 2, which was used to manufacture DHA, Artemether, and Artesunate. Building 2 had a changing area, including a crossover bench, a toilet, and a hand-washing facility. The visitors were required to wear shoe covers, a coat, and a hairnet. The layout of Building 2 was reviewed and spread over two floors, i.e., the first floor and the second floor. The first floor has a common personnel entry for three API manufacturing areas. Artemether was manufactured on the first floor, while DHA and Artemisinin (artesunate) were produced on the second floor. The second floor had separate synthesis and cleanroom areas for DHA and Artesunate. Before the crude DHA/ethanol clear solution was transferred from the dissolution tank to the cleanroom through an SS line, the solution was filtered through a 0.45µm filter. The mother liquor was collected in a separate tank, and the ethanol was recovered through distillation. The recovered ethanol was not reused in the DHA manufacturing process, and it was handled by both an in-house EHS team and a third-party vendor. The inspector visited the cleanroom area where crude DHA was crystallized, centrifuged, dried, and packed. The area was generally maintained adequately.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

8. Packaging and identification labelling of APIs and intermediates

The packaging area was inspected, and it was generally well-maintained.

9. Storage and distribution

The inspection team visited warehouse number 2, which was used to store incoming Artemisia leaves. The bags containing Artemisia leaves were stored off the floor, and the batch number was assigned based on the number of trucks that delivered Artemisia leaves. One batch number was assigned to one truck. A 100- to 400-gram sample was collected from each bag, and a composite of approximately 1,000 grams was used for testing purposes. Based on the production plan/order received by the warehouse, a unique batch number was assigned to the Artemisia leaves consignment and then transferred to Building 1 through trollies and trucks. A floor balance was used to verify the quantity of Artemisia leaves. Dedicated personnel transferred and unloaded Artemisia's leaves on the 3rd floor. Building one was dedicated to manufacturing Artemisinin. The 2nd floor features 12 extraction tanks, where petroleum ether was used to extract Artemisinin from Artemisia leaves.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

10. Laboratory controls

The QC lab (wet chemistry, microbiology lab, and instrument lab) was located on the third floor of building number 7. Additionally, the QA office, archive room, retention sample room, and stability chambers were all located on the same third floor. The laboratory was equipped with four HPLCs, two GCs, a UV-VIS spectrometer, a FTIR spectrometer, a pH meter, a KF apparatus, analytical balances, and other necessary equipment. The chromatographic instruments were connected to the LAN, and the date/time stamp was locked.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

11. Validation

The validation master plan for 2024 was only available in Chinese.

Computer system validation

The computerized system list for production equipment dated was reviewed. The list provided details such as equipment name, ID, type, used for, location, software version, level of access privileges, printer function available, data storage function available, and GAMP category (1, 3, 4 & 5). A similar list was available for QC equipment. The production software was categorized as GAMP 3, whereas most QA equipment was categorized as GAMP 4. The SOP for managing computerized systems was reviewed, providing purpose, scope, responsibilities, definition, and procedure. The procedure described how activities related to computerized systems, such as passwords, access control, backup, data archiving, recovery, and other aspects, were managed. For the validation of the computerized system, a separate SOP-10-037 was cross-referenced in this SOP.

Cleaning validation

The SOP for cleaning validation was available. The global approach for cleaning validation included visual inspection, testing of chemical residues, cleaning agent residues, and microbial limits. The equipment was cleaned after each batch. The Allowable Residue Limit (ARL) was calculated using five methods: 10 ppm residue, 1/1000 of the lowest daily dosage for intake, the LD_{50}, PDE (Permissible Daily Exposure level), and the NOEL (No Observed Effect Level). The lower result was kept for the cleaning validation. There were two sampling methods: rinsing samples or swabs. The location of the sample was indicated in the validation plan.

Process validation

The process validation of Artemisinin was reviewed, and it was noted that the process was last revalidated for crude Artemisinin using three batches. For refined Artemisinin, it was revalidated, taking three batches. The process validation of DHA was reviewed, and it was noted that the process was last revalidated for crude DHA, using three batches in January 2024. Non-micronized DHA was revalidated, taking three batches in Sept-Oct 2023. The micronized DHA was revalidated, taking three batches in Sept 2021.

Analytical method validation

Analytical method validation for micronized and non-micronized DHA was performed in November 2022 for assay and related substance tests.

Temperature mapping

An external service provider performed temperature mapping for retention sample rooms 1 and 2 in December 2019. The company confirmed that the temperature mapping was performed for all stability chambers connected to an alarm and messaging system. Temperature mapping was performed for three temporary storage areas/warehouses on the first floor of Building 2, which are used to store DHA, Artemether, and Artesunate. The area was equipped with a messaging system. The temporary storage area on the 2nd floor was used to store raw and starting materials.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

12. Change control

The SOP for change control was reviewed and found acceptable. The QA was responsible for categorizing the change. The list of changes for 2024 was provided. A total of 13 changes were initiated. All changes were categorized as minor.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

13. Rejection and re-use of materials

Reprocessing and reworking

The SOP for reprocessing and reworking APIs was discussed. The procedure described terms such as reprocessing and reworking, and also described the steps for reprocessing DHA, Artemether, Artesunate, Artemisinin crude, and Artemisinin. The procedure stated that rework should be fully understood before its application, and rework required concurrent validation of the process. The reworked batch was subjected to a stability study, and a batch number with a unique letter was appended to differentiate it from the initial batch and the reprocessed or reworked batch. The company confirmed that there has been no reprocessing or reworking since 2021.

Recovery of solvents

The SOP for solvent recovery management was discussed, which guided the recovery and reuse of solvents in the production department, including petroleum ether, acetone, petroleum ether/ethyl acetate, ethyl alcohol, methanol, and dichloromethane. The solvents were recovered within the production facility using a distillation process; therefore, a separate recovery facility was not available. It was confirmed that the external party was not involved in recovering any solvents. Each recovered solvent was assigned a unique batch number, and separate specifications were available for recovered solvents.

14. Complaints and recalls

The SOP for customer complaints was reviewed. The procedure was applied to complaints related to quality, whereas adverse reactions were handled through a separate procedure. The QA was responsible for handling the complaint within two working days of receiving it. The procedure stated that, except for "invalid complaints," the quality manager shall formulate handling measures. A separate procedure was followed for root cause analysis, which included methods such as brainstorming, fishbone diagrams, 5-Why analysis, fault tree analysis, and other techniques.

Product recall

The SOP for product recall was reviewed. Based on the risk assessment, the recall was classified into three categories. The company confirmed that there had been no recalls since the last PQ inspection. The DHA was mainly supplied within China, whereas Artemisinin was also exported; hence, the mock recall performed in 2022 considered Artemisinin. From the procedure, it was noted that a mock recall was conducted once a year, typically in December, if no actual recall had occurred. The mock recall for domestic and international markets was performed alternately.

15. Contract manufacturers (including laboratories)

It was declared that no contracted manufacturing operation existed. Regarding the Quality Control laboratory testing, the SOP "Control laboratory management" was available. Four contract laboratories were identified for contracted testing. A technical agreement was presented and was valid for one year.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ 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, ***CR SanJiu (Youyang) Pharmaceutical Co., Ltd***, located at ***108, Southern Jinyuan Road, Banxi Light Industry Area, Youyang City, Chongqing, China*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines for APIs.

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

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

Part 4	List of GMP Guidelines referenced in the inspection report

1. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2. ***Short name: WHO TRS No. 957, Annex 2***
   http://www.who.int/medicines/publications/44threport/en/

2. 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/

3. 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

4. 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

5. 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

6. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1.
   Short name: WHO TRS No. 957, Annex 1
   http://www.who.int/medicines/publications/44threport/en/

7. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3.
   Short name: WHO TRS No. 957, Annex 3
   http://www.who.int/medicines/publications/44threport/en/

8. 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

9. 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

10. 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

11. 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

12. 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

13. 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/

14. 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/

15. 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

16. 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

17. 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

18. 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 Multisource guidance or ***WHO TRS No. 996, Annex 10***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

19. 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/

20. 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

21. Production of water for injection by means other than distillation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 3.
Short name: WHO TRS No. 1025, Annex 3
https://www.who.int/publications-detail/978-92-4-000182-4

22. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4.
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