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Prequalification Unit Inspection services
WHO PUBLIC INSPECTION REPORT

Active Pharmaceutical Ingredient Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	Qinhuangdao Zizhu Pharmaceutical Co Ltd
Corporate address of manufacturer	No.10, Longhai Road, Economic & Technological Development Zone, Qinhuangdao, Hebei Province, P. R. China
Name & Address of inspected manufacturing site if different from that given above	Qinhuangdao Zizhu Pharmaceutical Co Ltd No. 10 Longhai Road, Economic & Technological Development Zone Qinhuangdao City, Hebei 066 004, China
Synthetic Unit /Block/ Workshop	• Synthesis plants #1 and #2 • Purification plant • Multifunctional plant 3
Inspection details	
Dates of inspection	1 – 4 July 2024
Type of inspection	Routine re-inspection
Introduction	
Brief description of the manufacturing activities	Production and quality control of intermediates and APIs.
General information about the company and site	Qinhuangdao Zizhu Pharmaceutical Co. Ltd. (QZP) is a wholly owned subsidiary of China Resources Zizhu Pharmaceutical Co., Ltd (CRZP). QZP located at the Qinhuangdao Economic and Technological Development Zone produces hormones APIs and intermediates for CRZP's finished products and export.
History of the regulatory inspections	The last WHO GMP onsite inspection was conducted on 15-19 October 2018. The site was regularly inspected by the Hebei Medical Products Administration.
WHO products covered by the inspection	• APIMF170 Mifepristone • APIMF171 Ethinylestradiol • APIMF172 Levonorgestrel

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	**Document reviewed:** • Quality management • Personnel • Buildings and facilities • Process equipment • Documentation and records • Materials management • Production and in-process controls • Packaging and identification labelling of APIs and intermediates • Storage and distribution • Laboratory controls • Validation • Change control • Rejection and reuse of materials • Complaints and returns • Contract laboratories **Site area visited:** • Production blocks: Synthesis and purification plants • Warehouses for starting materials and finished APIs • QC laboratory—Physical and chemical • Water system • HVAC
Restrictions	The scope of the inspection was restricted to the API in the WHO PQ programme.
Out of scope	APIs which are not under the scope of prequalification.
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
BER	Batch Analysis Record
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	Nonconformity
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
QP	Qualified person
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
WFI	Water for injection

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

1. Quality management

A system for managing quality that involved participation of management and appropriate manufacturing personnel was in place. Quality-related activities were defined and documented. The Quality department was independent of the production department. Persons authorized to release intermediates and APIs were specified. Quality-related activities were recorded at the time they were performed. Deviations from established procedures were documented and explained. Regular internal audits were performed in accordance with an approved schedule.

Product Quality Review (PQR)
Regular quality reviews of APIs were conducted, reviews were evaluated, and an assessment made of whether corrective action or any revalidation was required undertaken.

The "Product quality review management procedure" was checked. According to the SMP, PQR was performed annually covering all released batches from January to December. For the same API, PQRs were prepared based on manufacturing processes. The statistical tools were applied for process capability evaluation. Generally, SMP was well written and covered all required items. The 2023 APQRs for Levonorgestrel, Mifepristone and Ethinylestradiol were checked and discussed.

Deficiencies raised in this section have been addressed satisfactorily.

Quality risk management
The "Quality risk management procedure" and "Examples for Risk assessment reference" were verified. Common tools including flow charts, fishbone diagrams, failure mode and effect analysis (FMEA), risk ranking and selection, statistical tools, etc. were among the quality risk management techniques and tools utilized. The RPN acceptance criteria for quantitative risk assessment was defined. Performed risk assessments were recorded in a logbook.

Management review (MR)
The "Quality system review management procedure" was checked. According to the procedure MR should be performed annually. Last MR was performed in Feb 2024. The List of participants and the MR report were presented and checked.

Internal audit
The "GMP Internal audit management procedure" was checked. According to the procedure a comprehensive internal audit should be performed periodically. Requirements for audit team were specified. System-based check lists were used to perform audits and record findings. The last audit was carried out in April 2024. The audit report was approved by the QP. CAPAs were proposed by audited departments; CAPA implementation was evaluated by QA.

Product release
Intermediates and finished APIs products were released following "Batch review and release management procedure". The product release was the responsibility of the QP and was delegated to specified QA staffs. The batch release for a Levonorgestrel batch was checked.

Deficiencies raised in this section have been addressed satisfactorily.

Data integrity
The list of computerized systems was presented. HPLC/UPLC/GC were connected to computerized systems by applicable software. IR and Laser particle size tester were stand-alone instruments. The following procedure explained the general principles for QC computerized systems were checked and discussed.

- "Computerized system privileges management procedure"
- "QC computerized system management procedure"
- "Waters network connected HPLC operation procedure"
- "Computer system back-up and data restoration management procedure"
- "Business continuity procedure"

2. Personnel

An organizational chart was available. The key personnel of the various department had pharmaceutical qualification and were experienced in pharmaceutical manufacturing. The Quality unit was independent from Production unit. Units' responsibilities were described in writing. Number of personnel according to the company presentation totaled 320.

Job descriptions

Responsibilities of personnel engaged in the manufacture of intermediates and APIs were specified in writing. The following were checked:

- "Qualified person job description"
- "QC supervisor job description"
- "Deputation procedure for QA and QC personnel"

Training

An adequate number of qualified, trained, and experienced personnel was available. All employees were subject to regular training according to the company's training procedure and annual training plan.

The "GMP training management procedure" and "Analyst training management procedure" were checked. Annual training plan for 2024 was available. Training effectiveness was evaluated.

Hygiene

Direct contact with intermediates and APIs was avoided. Smoking, eating, drinking, chewing and the storage of food were restricted. Personnel with an infectious disease or who have open lesions on the exposed surface of the body were not engaged in activities that could result in compromising the quality of APIs.

"Workshop hygiene management procedure" was checked. All employees were required to pass the annual health examination and additional occupational health and disease checks.

3. Buildings and facilities

Design and construction

During the site tour the following facilities were visited:

- Warehouses
- Synthesis plant #1 and #2
- Multifunctional plant #3
- Purification plant
- PW system
- HVAC system

In general, the facilities were located, designed, and constructed to facilitate cleaning, maintenance and operations as appropriate to the type and stage of manufacture. Adequate space was provided for the orderly placement of equipment and materials. The flow of materials and personnel through the building was appropriate to prevent mix-ups or contamination.

Purified water system (PW)

PW was generated from pretreatment of drinking water followed by RO, UV and 0.22 µ filter to the storage tank and loop. Conductivity, pH, and some other parameters were monitored on-line, TOC was determined offline at QC. The PW system was provided with an alarm system. The loop was in continuous circulation. The storage tank and circulation loop sanitization were performed regularly. PW trends for 2023 were checked for PW system located in the purification plant. All results were below the alert limit.

HVAC system
In class D rooms, the filter cascades were established for air supply and exhaustion. Fresh air was used. HEPA filters were installed in the rooms. Pressure differentials were monitored between filters. The "Operation manual of AHU" and "Utility supply management procedure" were discussed.

QC laboratories
QC laboratories visited were seen to be spacious, in good order and clean.

Environmental monitoring (EM) programme
The "HVAC system routine monitoring management procedure" was checked. According to the SMP temperature, RH, and pressure differentials were monitored and recorded. Microbiological monitoring was done monthly for the "clean rooms" used for Mifepristone, Ethinylestradiol and Levonorgestrel production. EM trends for Levonorgestrel production "clean rooms" for 2023 were checked. All results were below the alert limit.

Lighting
Adequate lighting was provided in all areas to facilitate cleaning, maintenance, and proper operations.

Sanitation and maintenance
In general buildings used for the manufacture of intermediates and APIs were properly maintained and kept in a clean condition. Written procedures were established. The responsibilities for sanitation were defined and the cleaning schedules, methods, equipment, and materials to be used for cleaning buildings and facilities described.

4. Process equipment

Design and construction
Equipment used in the manufacture of intermediates and APIs was not dedicated. Generally, equipment was of appropriate design size, and suitably located for its intended use, cleaning, sanitization and maintenance. Equipment and permanently installed processing lines used during the production of an intermediates or API were appropriately identified, calibration due dates were specified on each equipment as well as cleaning status and cleaning certificates were available.

Equipment maintenance and cleaning
Schedules and procedures were established for the preventive maintenance of equipment. Written procedures were established for cleaning of equipment and its subsequent release for use in the manufacture of intermediates and APIs. The following documents were checked, but not limited to:

- "Levonorgestrel production equipment operation procedure"
- Cleaning procedure for reactors
- The maintenance and cleaning record of a centrifuge.

Calibration
Control, weighing, measuring, monitoring, and test equipment were calibrated according to written procedures and an established schedule. Equipment calibrations were performed using standards traceable to national standards. The current calibration status of critical equipment was known and verifiable.

Computerized systems
Computerized systems were not used in production and material management. GMP-related computerized system was used in QC lab. The validation of computerized system was not checked in this inspection due to time constraints.

5. Documentation and records
Documents related to the manufacture of intermediates or APIs were prepared, reviewed, approved, and distributed according to written procedures. The issuance, revision, superseding and withdrawal of all documents were controlled and revision histories maintained. A procedure was established for retaining documents, the retention periods for documents were specified.

Production, control, and distribution records and records of major equipment use, cleaning, sanitization, and maintenance were retained following written procedures. Laboratory control records included complete data derived from all tests conducted to ensure compliance with established specifications and standards; traceability was ensured.

Batch numbering system
The "Batch numbering system" was checked. A reprocessed/reworked batch was referenced in the batch number. The codes for WHO PQed APIs were discussed.

Equipment cleaning and use record
Records of major equipment use, cleaning, sanitization and maintenance showed the date, time, product and batch number of each batch processed in the equipment, and the person who performed the cleaning and maintenance.

Records of raw materials, intermediates, API labelling and packaging materials
Records of raw materials, intermediates, API labelling and packaging materials were maintained including, but not limited: name of manufacturer, quantity supplied, name of supplier, number allocated upon receipt and date of receipt.

Master production instructions
Master production instructions were prepared, dated, and signed by one person and independently checked, dated, and signed by a person in the quality unit. Master production instruction contained detailed production instructions.

Batch production records
Batch production records included complete information relating to the production and control of the batch. The batch production record was checked before issuance. Records were numbered with a unique batch or identification number, dated and signed when issued.

Laboratory control records
Laboratory control records included complete data derived from all tests conducted to ensure compliance with established specifications and standards. Records were maintained for modifications to an established analytical method, periodic calibration of laboratory instruments, apparatus, and recording devices, stability testing performed on APIs and OOS investigations.

Batch production record review
Written procedures were established for the review and approval of batch production and laboratory control records, including packaging and labelling. Batch production records of critical process steps were reviewed and approved by the quality unit before an API batch was released or distributed.

6. Materials management

Written procedures describing the receipt, identification, quarantine, storage, handling, sampling, testing and approval or rejection of materials were available. Changing the source of supply of critical raw materials was according to the change control procedure.

Supplier management
The "Supplier management procedure" was checked and found to be acceptable.

Warehouses (WHs)
Solid raw materials and liquids WHs were visited during the site tour. Warehouses were found clean and materials placed in good order. Materials management was paper based, was checked and was found in good order. T & RH requirements for room where WHO APIs were stored were defined. Temperature (T) and RH were monitored and recorded.

The "Sampling management procedure" and "Sampling operation procedure" were checked. SMPs were applicable to all materials sampling including water. For primary packaging materials, sampling was done in QC in classified area. A simple sampling booth was used for non-toxic solid materials sampling. Sampling and dispensing of KSM was done in LAF booth. All material sampling was performed by QA personnel.

7. Production and in-process controls

Raw materials used for manufacturing of intermediate and API were weighed/measured under appropriate conditions. Weighing and measuring devices were of suitable accuracy for the intended use. Critical weighing, measuring, and other critical operations were witnessed. Actual yields were compared with expected yields. Deviations were documented, critical deviations were investigated. The processing status of equipment was indicated. Written procedures were established to monitor the progress and control the performance of processing steps. In-process sampling was carried out following established procedures.

Blending batches of intermediates or APIs
The "API and Intermediate blending management procedure" was in place. Blending operation for Levonorgestrel API was performed before micronization.

Contamination control
Production operations were conducted in a manner that prevented contamination of intermediates or APIs by other materials.

8. Packaging and identification labelling of APIs and intermediates

Written procedures describing the receipt, identification, quarantine, sampling, examination and/or testing and release and handling of packaging and labelling materials were available. Records were maintained for each shipment of labels and packaging materials.

Label issuance and control

Access to the label storage areas was limited to authorized personnel. An established procedure to guide the reconciliation of quantities of labels issued, used, and returned and to evaluation of discrepancies between the number of containers labelled and the number of labels issued. A printed label representative of those used was included in the batch production record.

Packaging and labelling operations

Procedures were available to ensure that the correct packaging materials and labels were used. Line clearance procedure was in place.

9. Storage and distribution

Warehousing procedures

Facilities were available for the storage of materials and API products under appropriate conditions. Designated areas were available for quarantine, rejected, returned, or recalled materials.

Distribution procedures

APIs and intermediates were distributed to third parties after they had been released by the quality unit. Special transport or storage conditions for an API or intermediate were stated on the labels. A system was in place by which the distribution of each batch of intermediate and/or API can be readily determined to permit its recall.

10. Laboratory controls

Procedures were in place describing sampling, testing, approval, or rejection of materials and recording and storage of laboratory data. Specifications and sampling plans were available. Laboratory records were maintained. Laboratory controls were followed and documented at the time of performance. Departures from procedures were documented and explained. OOS results obtained were investigated and documented according to a procedure.

Reagents and standard solutions were prepared and labelled following written procedures, and expiry dates (use by) were applied.

Primary reference standards were obtained as appropriate for the manufacture of APIs. The source of each primary reference standard was documented. Records were maintained of each primary reference standard's storage and use. Secondary reference standards (working standards) were appropriately prepared, identified, tested, approved, and stored.

Control, weighing, measuring, monitoring, and test equipment were calibrated according to written procedures and an established schedule. Equipment calibrations were performed using standards traceable to certified standards. Records of calibrations were maintained. The current calibration status of equipment and instruments was indicated.

Certificate of an analysis (CoA)

The "Raw test record and CoA management procedure" cross-checked with the demonstrated process during the QC visit. Raw data from test records was entered into the CoA by a designated person from QC, re-checked by a second designated person from QC and reviewed/approved by QC supervisor or designee.

Stability monitoring of APIs

The "Stability management procedure" was checked. Stability samples were stored in containers that simulate the market container.

Expiry and retesting dating
Supporting stability information was available to assign the expiry or retest date.

Reserve/retention samples
The reserve samples were stored in the same packaging system in which the API was stored. The SOP for "Management of retained samples" was checked. According to the SOP in case a product was released according to the different specifications, representative samples had to be stored. Visual inspection of retained samples was done annually.

Data management
QA was responsible for data review of finished APIs; QC was responsible for data review of starting materials and intermediates. Electronic data and audit trails were randomly checked by QC supervisor on a regular basis. The following procedures were checked:
"QC data review procedure"
"Chromatographic instruments data acquisition, processing and reporting procedure"
"Chromatographic column management procedure"

OOS management
The "Management procedure of OOS/OOT results investigation" was checked. SMP was applicable to all OOS/OOT test results:

- Raw materials
- Packaging materials
- Intermediates
- Finished products
- Utility systems,
- Stability studies

OOS/OOT trending was performed quarterly. Trends for 2023 and 2024 (1st quarter) were presented. OOS/OOT logbooks for 2023 and 2024 were presented. Several OOSs were checked and discussed.

11. Validation
The company's overall policy, intentions and approach to validation was explained in VMP. The "Validation Master Plan" was verified.

Process Validation
Process validation was performed following the "Validation management procedure". Validation protocols specified critical process steps, batch size, and acceptance criteria as well as the type of validation to be conducted and the number of process runs. Validation reports that cross-reference the validation protocol were prepared, summarizing the results obtained, commenting on any deviations observed, and drawing the appropriate conclusions. The process validation of proposed process for Levonorgestrel API under WHO assessment, PV of Levonorgestrel blending and PV of Levonorgestrel micronization were checked and discussed.

Qualification
Before validation activities, appropriate qualification of critical equipment and ancillary systems was completed.

Periodic review of validate systems
According to the VMP systems and processes were periodically evaluated to verify that they are still operating in a valid manner.

Cleaning validation
Cleaning validation was carried out as per the validation master plan. Swab and rinse sampling methods were required to be used. The protocol and report of "Levonorgestrel production equipment cleaning validation" were discussed. The relevant analytic method was validated, and the report was approved. LOD and LOQ appeared appropriate compared with the residue limit.

Analytical method validation
The analytical method validation report for EI testing in Levonorgestrel performed by an external laboratory was checked and discussed.

Deficiencies raised in this section have been addressed satisfactorily.

12. Change control (CC)
The "Change management procedure" was checked. Changes were classified as:
- Permanent
- Temporary
- Major
- Medium
- Minor

The "change of Levonorgestrel manufacturing process" and the change associate action plan were checked and discussed.

Deviations
The "Deviation management procedure" was checked. Summary of deviations were discussed in MR meeting. Deviations were classified as:
- Minor
- Major
- Critical,

CAPAs were to be initiated in accordance with the procedure. Trends for 2023 and 1st quarter of 2024 were presented. Deviation registers for 2024 was checked. In general deviation SMP and handling of deviation investigations were appropriate.

CAPA
The procedure "CAPA management procedure" was checked. SMP was applicable, but not limited to all the life cycle of products, R&D, technology transfer, commercial production, deviations, self-inspection, external audits, complaints, OOS, and recalls. CAPA logbook for 2024 was checked.

Deficiencies raised in this section have been addressed satisfactorily.

13. Rejection and re-use of materials
Rejection
The "Management Procedure for rejected products of starting materials, packaging material, intermediates and APIs" was in place. The rejection register for 2024 was checked.

Reprocessing and reworking

The "Reprocessing and Reworking of APIs and intermediates" was checked. The reprocessing register was maintained and checked.

Recovery of materials and solvents

A procedure for recovery of materials and solvents of APIs and intermediates was in place. The "Solvents recycle and recovery management procedure" was checked. The use of recovered solvents was discussed.

Return

The procedure for returned APIs and intermediates was in place. The "Management procedure for returned product" was discussed. Returned intermediates or APIs were identified as such and quarantined. The return register 2023 was in place and checked.

Deficiencies raised in this section have been addressed satisfactorily.

14. Complaints and recalls

Quality-related complaints were recorded and investigated according to a written procedure. Records of complaints were retained in order to evaluate trends, product-related frequencies and severity with a view to taking additional, and if appropriate, immediate corrective action. A written procedure that defined the circumstances under which a recall of an intermediate or API was considered was available.

The "Complaints management procedure" and the flow chart were checked. QA was responsible for the investigation of received complaints. Complaints were classified as:

- Major
- Minor

According to the SMP trending should be performed annually. No complaints were received in 2024, one complaint was received in 2023.

The "Recall procedure" and the flow chart were checked. Recall classification:

- Class I – recall within 24 hours
- Class II – recall within 48 hours
- Class III – recall within 72 hours

SMP effectiveness was evaluated by mock recall every two years. Last mock recall was performed in 2023 for the domestic market.

15. Contract manufacturers (including laboratories)

Contract laboratories were evaluated according to a written procedure. Written and approved contracts/agreements between the company and the contract acceptor that defined GMP responsibilities, including the quality measures, of each party were available. Contracts permitted the contract giver to audit the contract acceptor's facilities. The technical agreements (contracts) were checked for contract testing by external testing laboratories.

Part 3	Initial 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, ***Qinhuangdao Zizhu Pharmaceutical Co Ltd*** located at ***No. 10 Longhai Road, Economic & Technological Development Zone Qinhuangdao City, Hebei 066 004, 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 GMP 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

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 TRS No. 957, Annex 2

3. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3.
   Short name: WHO TRS No. 1033, Annex 3

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

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

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

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 TRS No. 961, 957), Annex 1

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 3.
   Short name: WHO TRS No. 957, Annex 3

9. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-sixth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 2.
   Short name: WHO TRS No. 1044, Annex 2

10. WHO guidelines on technology transfer in pharmaceutical manufacturing. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-sixth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
    Short name: WHO TRS No. 1044, Annex 4

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

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

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

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

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

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

17. Good Manufacturing Practices: Guidelines on validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3.
Short name: WHO TRS No. 1019, Annex 3

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

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

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

21. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4.
Short name: WHO TRS No. 1033, Annex 4

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

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

24. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-third Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1019), Annex 2.
Short name: WHO TRS No. 1019, Annex 2

25. Points to consider when including Health-Based Exposure Limits in cleaning validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 2.
Short name: WHO TRS No. 1033, Annex 2

26. Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 6.
Short name: WHO TRS No. 1025, Annex 6

27. 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

28. 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.
Short name: WHO TRS No. 1025, Annex 4

29. WHO good practices for research and development facilities of pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-sixth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 6.
Short name: WHO TRS No. 1044, Annex 6

30. WHO good manufacturing practices for investigational products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-sixth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 7.
Short name: WHO TRS No. 1044, Annex 7

31. WHO good manufacturing practices for excipients used in pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052), Annex 2.
Short name, WHO TRS No. 1052, Annex 2