20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

Prequalification Unit Inspection Services
WHO PUBLIC INSPECTION REPORT

Active Pharmaceutical Ingredient Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	Jiangsu Lianhuan Pharmaceutical Co., Ltd.
Corporate address of manufacturer	No.9, Jiankangyi Road, Biological Health Industry Park, Yangzhou, Jiangsu Province, 225127, China
Name & Address of inspected manufacturing site if different from that given above	Same as above
Synthetic Unit /Block/ Workshop	Production line C7-H5, Production line C4-H3 No. 6 Clean Area in Building C4
Inspection details	
Dates of inspection	10 to 13 March 2025
Type of inspection	Initial inspection
Introduction	
Brief description of the manufacturing activities	Production and quality control of intermediates and APIs, small volume parenteral products, tablets, hard capsules, suppositories, granules, gels, and oral solutions
General information about the company and site	The company was founded in 1958. The site occupied an area of approximately 130,000 square meters, with a building area of about 150,000 square meters. There are four production workshops, including two active pharmaceutical ingredient (API) workshops, one solid dosage workshop, and one liquid dosage workshop. The company employs approximately 938 staff members. According to the company information, other potent API and highly allergenic, cytotoxic or cytostatic APIs were not manufactured on the site.
History of the regulatory inspections	This was the initial onsite inspection performed by WHO. The site was inspected by US FDA in July 2024 for different scope of products.
WHO products covered by the inspection	Levonorgestrel (APIMF484, WHOAPI-484)
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	**Documents 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 areas visited:** • Production blocks • Warehouses for starting materials and finished APIs • QC laboratory—Physio-chemical and Microbiological • Water system • Compressed air / Nitrogen plant • HVAC
Restrictions	The scope of the inspection was restricted to the facility related 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 documented system for quality assurance was established, with procedures covering key quality elements in place. The Quality Department was divided into QA and QC and were separate from the Production Department. Operations were specified in written form and critical GMP requirements were essentially being met. The procedures reviewed and discussed during the inspection were generally of an acceptable standard.

Product Quality Review (PQR)

Annual product quality review was performed following "Product quality review management procedure". According to the SMP, PQR was performed annually covering all released batches from January to December of the year. Several quality grades of Levonorgestrel API were manufactured at the site. The WHO grade of Levonorgestrel followed EP specifications with additional control of polymorph. The dossier was under assessment at the time of this inspection.

The following APQRs were checked:
Levonorgestrel APQR 2022
Levonorgestrel APQR 2023
Levonorgestrel APQR 2024

Quality risk management
The SOP Risk management procedure was available. Hazard and Operability approach (HAZOP) was used. Rating of risks was done including evaluation of Severity, Probability and Detectability and calculation of RPN. Quality risk management plan should be updated every year for every product according to the procedure. Plan for Levonorgestrel was updated in January 2025. Last Levonorgestrel life cycle risk assessment review performed in December 2024 was documented.

Risk assessment in relation to cross-contamination issues
The production area was physically separated from other areas. Production line and HVAC was dedicated. The risk assessment and control measures were checked during the inspection in the HVAC area. Measures for the prevention of cross-contamination by exhaust air from areas, rooms and processes were reviewed and discussed.

Nitrosamines
The company performed a risk assessment for nitrosamine impurity of Levonorgestrel in June 2022 and concluded there was no chemical structure risk that could introduce genotoxic impurities.

Management review (MR)
The "Quality system review management procedure" was checked. MR was required to be performed annually with attendance of senior management. The report for MR meeting held in January 2025 for the period of January to December 2024 was reviewed and discussed.

Internal audits
The company implemented the GMP self-inspection procedure and established a self-inspection team. An annual self-inspection plan was formulated to carry out regular self-inspections. Further details were not reviewed during this inspection.

Deviations
The "Deviation management procedure" was checked. The procedure was applicable, but not limited to material management, deviations that can impart product homogeneity, safety, effectiveness including deviations from GMP, MF, SOPs, specifications. Summary of deviations were discussed in MR meeting. A deviation was classified as minor, major or critical. Deviation registers for 2024 were available and checked.

CAPA
The "CAPA management procedure" was checked. The procedure was applicable, but not limited to production, deviations, self-inspection, external audits, complaints, OOS, and recalls. CAPAs were recorded and the CAPA register was maintained. The 2024 CAPA register and examples of CAPA were checked.

Product release
The "Finished product release procedure" was checked. The QP was responsible for the final review of all the relevant documents including BMR, BPR and batch testing record for the release of finished product according to the procedure. The batch release of WHO grade Levonorgestrel API was checked and discussed.

Data integrity
The "Data Reliability management procedure" was available. A full audit trail function must be enabled during installation for a system used for collection of process report and/or original electronic data according to the procedure.
The following documents were checked.

- "Analysis raw data/record management procedure"
- "Finished product, intermediate analysis procedure"

2. Personnel

An organization 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 the Production unit. Units' responsibilities were described in writing.

Job descriptions

Responsibilities of personnel engaged in the manufacture of APIs were specified in writing. The following job descriptions were checked and found to be generally acceptable.

- QA VP
- Qualified person job description
- QC manager
- Production VP

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 "Training management procedure" was checked. Training effectiveness was evaluated by oral and written tests and in practice. Annual training plan for 2024 was available. The implementation was monitored.

Hygiene

The "Workshop hygiene management procedure" was checked. All employees should pass an annual health examination and additional occupational health and disease checks. Direct contact with intermediates and APIs was avoided. Personnel with an infectious disease or who have open lesions on the exposed surface of the body were not engage in activities that could result in compromising the quality of APIs.

3. Buildings and facilities

Design and construction

Levonorgestrel was manufactured in the specified buildings. The Levonorgestrel production lines were dedicated.

During the site tour the following production facilities were inspected:

- Warehouses for raw materials, intermediates, packing materials, finished APIs.
- Production line for intermediate of Levonorgestrel and crude of Levonorgestrel
- Purification line and micronization of Levonorgestrel
- Inner packing area.

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. Entrance to production workshops was via a change room cascade and PAL (personal air lock), gowning procedures photos were displayed. Final steps were performed in D class "clean rooms". Premises visited were seen clean and properly maintained, entrances were controlled.

Terminal HEPA filters were installed in the ceilings of the cleanrooms. Traceability to the installation plans was ensured by appropriate numbering and labelling. Monitoring of humidity, temperatures and relevant pressure differences between rooms was ensured in the cleanroom area.

HVAC system
The production environment for the Levonorgestrel purification process was designed to fulfil requirements of cleanliness class D. The HVAC system was equipped with an independent horizontal combined air conditioning unit to purify and climate control the air. The airflow was top supply and lower side return. The installation area for the HVAC system was visited. An appropriate filter cascade was installed. Filter differential pressures were monitored. Logbooks were kept.

Purified water (PW) system
The water used of purified water came from drinking water produced by an urban water plant. The purified water production equipment was composed of multi-media filtration, softener, activated carbon filtration, precision filter, reverse osmosis device, electro deionization device, transfer pump (sanitary), PW storage tanks and 316 stainless steel circulation pipelines. The PW system relevant to the Levonorgestrel production was inspected.

Nitrogen preparation system
Nitrogen preparation system was inspected. Documents for qualification and requalification, including specifications and monitoring results, were reviewed

Compressed air
Compressed air preparation system was installed and used for Levonorgestrel micronization operation. Documents for qualification and requalification, including specifications and monitoring results of compressed air, were reviewed

QC laboratories
The quality control department was housed in a building that provided sufficient space for QC activities, including the storage of retained samples and product samples for stability programmes.

Environmental monitoring (EM) programme
The “Non-sterile API clean area environmental monitoring procedure” was verified. Monitoring frequency was described. Evaluation was done in the APQR Levonorgestrel API. It was summarised, that all results for EM of the clean area met requirements.

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

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

4. Process equipment

Design and construction
Equipment used in the manufacture of intermediates and the API was dedicated. Generally, equipment was of appropriate design and adequate size, and suitably located for its intended use, cleaning, sanitization, and maintenance. Equipment and permanently installed processing lines used during the production of intermediates or APIs were appropriately identified, calibration due date was specified on each equipment as well as cleaning status and cleaning certificate.

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 cleaning procedure for Levonorgestrel equipment was reviewed.

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 certified 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 systems were used in the QC laboratory. The procedure for "Computerized system management" was checked.

5. Documentation and records

Documentation was designed, prepared, reviewed, and distributed according to "Document management procedure". Maintenance period of documents was defined in the procedure.

Documents related to the manufacture of intermediates or APIs were prepared, reviewed, approved, and distributed were spot checked. Production, control, and distribution records were retained for at least one year after the expiry date of the batch. For APIs with retest dates, records were retained for at least three years after the batch was completely distributed.

Batch numbering system

The "Procedure for production batch number preparation, use and management" and "Product Code procedure" were checked. A reprocessed/reworked batch was referenced in the batch number.

Equipment cleaning and use record

Records of major equipment use, cleaning, sanitization and maintenance contained the date, time, product and batch number of each batch processed in the equipment, and the person who performed the cleaning and maintenance. The cleaning records were kept separately from the BMR and archived by the production department. Additional documentation for the cleaning was done in the equipment use log.

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.

Batch production records

Batch production records included information relating to the production and control of the batch. The issuance of working copies of batch production record followed the procedure "Empty record printing, release, fill and return and maintenance". The authorized master formulae were available for products. Batch manufacturing records (BMRs) were retained for each batch processed.

Laboratory control records

The laboratory control records were linked to batch number. The laboratory control records included complete data derived from all tests conducted including OOS investigation were checked and discussed.

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. The following material receiving procedures were available:

- Chemical raw material receiving, storage and distribution procedure
- API finished product receiving, storage and distribution procedure.

Correct storage conditions and retest dates have to be checked before distribution. Shipments will be handled by the import/export department after release from the warehouse.

Supplier management

Supplier management procedure was available and reviewed during the inspection. SOP covered raw material suppliers and service providers. List of approved suppliers and service providers was available. Audit to critical raw material suppliers were performed following the procedure.

Storage of starting materials.

The warehouses for solid raw materials and liquids storage were inspected. They appeared clean and materials were placed in good order. Materials management was paper based. Check lists were used for materials receipt.

Storage of intermediates / finished product

Warehouses and storage area for intermediates and finished products were inspected, including cool warehouse, normal temperature warehouse, packaging material warehouse, returned product warehouse, non-conforming product warehouse etc. Temperature and humidity control requirements were defined and monitored for different storage rooms. The storage rooms used for Levonorgestrel intermediate and Levonorgestrel finished product were dedicated.

Inventory cards and CoAs for the finished API were available at the warehouse area. Before release of deliveries of finished API to external customers, a review and release sheet was filled.

7. Production and in-process controls

Raw materials for manufacturing of intermediate and API were weighed/measured under appropriate conditions. Weighing and measuring devices were of suitable accuracy for the intended use. 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 and testing were carried out. Actual yields were documented. Deviations in production control were required to be documented; critical deviations were investigated.

Contamination control

The manufacturing facility was dedicated for Levonorgestrel API production. 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 for labelling of APIs were available. Records were maintained for each shipment of labels and packaging materials.

Label issuance and control

Procedure was available to reconcile the quantities of labels issued, used, and returned and to evaluate discrepancies found 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. A line clearance procedure was in place.

9. Storage and distribution

Warehousing procedures
Facilities were available for the storage of materials 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 have 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

Sample receipt, handling, and testing
Samples from APIs and raw materials were handled according to the sample management procedure. Logbooks for sample receiving of raw materials and finished API products were maintained in the sample receiving area.

QC department performed all sampling for the APIs in the clean production area. Finished product sampling procedure and intermediate sampling procedure were available and checked.

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.

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.

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

Reference standards
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. Appropriate storage and handling were assured.

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. Analytical records for last revalidation batches were available and reviewed.

Stability monitoring of APIs
The "Stability management procedure" was implemented. Stability chambers were installed in the stability laboratory. Accelerated (40 °C/RH 75 %) and long-term stability studies (30 °C/RH 75 %) were initiated.
Calibration of stability chambers was done by an external service provider.

OOS management
The "Procedure for OOS investigation and handling" was checked. OOS register 2024 was maintained and checked. The entire investigation should be finalized within specified working days. There was no OOSs for Levonorgestrel API reported.

11. Validation

Validation master plan
An approved VMP and "Validation Master Plan 2025 were available. The company's qualification and validation policy and programme were defined and documented, including deviation management, change control, risk management principles.

List of computerised systems was not part of the VMP. A separate document "Computerised system management procedure" was in place. The validation of computerized system was not checked in detail in this inspection due to time constraints.

Process Validation
Process validation was performed following the "Validation management procedure". The validation protocol and validation report of Levonorgestrel API under WHO assessment was checked.

Qualification
Before validation activities, appropriate qualification of critical equipment and ancillary systems was completed by following SOP: Facility and equipment validation procedure. Requalification frequency of HVAC, PW, WFI, Compressed air, Nitrogen system and QC instruments was defined and checked.

Cleaning validation
The procedure for cleaning validation was available. Cleaning validation was carried out as per the validation mater plan. Swab and rinse sampling methods were required to be used. The protocol and report of "Levonorgestrel production equipment cleaning validation" were verified. Details of Levonorgestrel equipment cleaning SOP were checked.

Analytical method validation
Analytical methods validation and verification management procedure was available. Report for analytical method validation of Levonorgestrel equipment cleaning residue was reviewed.

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

12. Change control (CC)

The procedure for changes control management was checked. Changes were classified as:

- Permanent
- Temporary
- Major
- Medium
- Minor

A change control related to Levonorgestrel API was checked.

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 registers 2024 was checked. No Levonorgestrel related rejection was reported.

Reprocessing and reworking

The procedure for "Reprocessing and reworking of APIs and intermediates" was checked. The document was applicable to OOS intermediate and APIs.

Recovery of materials and solvents

The "Solvents recovery management procedure" was checked. The procedure allowed recovered solvents to be used in the same or different processes. The company claimed the solvent recovery was not applicable to Levonorgestrel API manufacturing.

Return

The "Management procedure for returned and recovered product" was reviewed. Returned intermediates or APIs were identified as such and quarantined. The returned product register was maintained and checked. There were no returned batches of Levonorgestrel reported.

14. Complaints and recalls

Complaints

The "Complaints management procedure" and a flow chart were checked. Quality-related complaints, when received were recorded and investigated according to a written procedure. Records of complaints were retained and evaluated; if appropriate, corrective action and preventive action were taken. Written procedure that defined the circumstances under which a recall of an intermediate or API was considered was available. Complaints were received and investigation was managed by QA responsible for quality system management. A complaint was classified as Major or Minor. Complaint registers 2024 was available and showed no complaints were received in 2024.

Recalls

The "Recall procedure" was checked. Recall classification:

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

The effectiveness of recall procedure was evaluated by mock recall every two years. Last mock recall performed in July 2024 was checked. According to the company information, there was no product recall in the past three years.

15. Contract manufacturers (including laboratories)

Contract production was not used for Levonorgestrel API. Contract labs were used for specified testing related to Levonorgestrel API. SOP about contract analyses was implemented. Technical agreements with contract laboratories were spot checked.

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 deficiencies listed in the Inspection Report, a decision on the compliance of ***Jiangsu Lianhuan Pharmaceutical Co., Ltd.*** located at ***No.9, Jiankangyi Road, Biological Health Industry Park, Yangzhou, Jiangsu Province, 225127, 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 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***

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***

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. 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***

7. 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***

8. 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***

9. 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**

10. 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***

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***

12. 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***

13. 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***

14. 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***

15. 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***

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**

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***

18. 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

19. 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***

20. 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

21. 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

22. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditionning 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***

23. 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***

24. 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***

25. 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***

26. 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***

27. 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***

28. 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***

29. 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***

30. WHO good practices for pharmaceutical quality control laboratories. 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 4***