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

Part 1	**General information**
Manufacturers details	
Name of manufacturer	Zhejiang East-Asia Pharmaceutical Co., Ltd.
Corporate address of manufacturer	Coastal Industrial City, Pubagang town, Sanmen County, Zhejiang (317100), P.R. China.
Inspected site	
Name & Address of inspected manufacturing site if different from that given above	Coastal Industrial City, Pubagang town, Sanmen County, Zhejiang (317100), P.R. China.
Unit /Block/ Workshop	• No. 11 workshop • No. 12 workshop
Inspection details	
Dates of inspection	23-27 October 2023
Type of inspection	Initial on-site inspection
Introduction	
Brief description of the manufacturing activities	Pharmaceutical manufacturing activities for non-sterile APIs and finished pharmaceutical products.
General information about the company and site	Zhejiang East-Asia Pharmaceutical Co., Ltd. was established in 1998. The site consists of the office area, the production facilities, the QC laboratories and the auxiliary area. The company is involved in research, development and manufacturing of APIs and finished pharmaceutical products. The non-sterile API categories produced on the site include quinolone antiseptic, anti-fungal, anti-spasmodic, antihistamine, and acetylcholinesterase, etc. No cephalosporin and penicillin products were manufactured on-site.
History	This was the first WHO GMP onsite inspection.
WHO products covered by the inspection	Levofloxacin Hemihydrate APIMF413
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	• Quality management system • Production blocks • Warehouses • QC laboratories • HVAC system • Water system
Restrictions	The scope of the inspection was restricted to the API in the WHO PQ programme.
Out of scope	Facilities used for the production of APIs other than Levofloxacin Hemihydrate were out of the inspection scope.

Abbreviations	Meaning
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
BAR	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 (where applicable)**

1. Quality management

A system for managing quality that involves 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 justified. Regular internal audits were performed in accordance with an approved schedule.

Product Quality Review

Regular quality reviews of APIs were conducted, reviews were evaluated, and an assessment made of whether any corrective action or any revalidation should be undertaken. The SOP "Product Quality Review procedure" was checked. Only three validation batches of WHO grade Levofloxacin Hemihydrate were produced.

Quality risk management

The SOP "Quality risk management" and SOP "Quality risk management plan" were checked. The risk assessment register for 2023 was available and recorded the risk assessments performed.

Management review (MR)

The SOP "Quality Management review" was checked. According to the SOP, management review should be performed annually to review quality system operations of the previous year. MR for 2022 was reviewed and found to be generally acceptable.

Product release

The SOP "Product release procedure" was checked. After analysis, analytical raw data (BAR), BMR, BPR and internal CoA were reviewed by QA. Final release was done by the QP or the persons authorized by the QP. The product release function was delegated to designated persons by following the SOP "Qualified person".

The SOP "Certificate of analysis template" was checked. CoAs were issued for each batch of intermediate or API. Final CoAs sent to the clients, were dated and signed by the QA manager or the QP.

Internal audit

The SOP "GMP self-inspection management" was checked. The SOP was applicable to all departments. Self-inspection was performed at least once per year. The schedule was presented to the inspector.

Electronic data management

The following SOPs/documents were checked and discussed.

- The SOP "Electronic data management"
- The SOP "Data integrity management"

- The SOP "QC laboratory system strategy and access rights"
- The SOP "Chromatographic data system"
- The SOP "Chromatographic integration management"

2. Personnel

An organization chart was available. Key personnel responsibilities were required to be defined in job descriptions. The key personnel of the various departments had pharmaceutical qualification and were experienced in pharmaceutical manufacturing.

The following job descriptions were reviewed and appeared acceptable.

- Head of production management
- Head of quality management
- Head of QC

Training

Adequate number of qualified trained and experienced personnel was available. The SOP "Personnel training" was checked. The 2023 training schedule was made available. Training effectiveness was evaluated. The QP's training file was briefly checked. The Analyst's competency list was made available to the inspectors.

Hygiene

The SOP "Personal hygiene" and SOP "Analysis work management" were checked. For new personnel, medical examinations were foreseen before joining the company and repeated yearly. Direct contact was avoided between the operator's hands and starting materials, primary packaging materials and intermediate or bulk product. Smoking, eating or drinking were forbidden in the production areas and the analytical laboratory. Personnel with an infectious disease or who have open lesions on the exposed surface of the body were not allowed to work with exposed product.

2. Buildings and facilities

Design and construction

The buildings and facilities inspected, were designed and constructed to facilitate cleaning, maintenance and operations as appropriate to the type and stage of manufacture. The buildings and facilities had adequate space for the orderly placement of equipment and materials to prevent mix-ups and contamination. The flow of materials and personnel through the building or facilities was designed to prevent mix-ups or contamination. Permanently installed pipework was appropriately identified.

Levofloxacin WHO grade was manufactured in the No.11 and No.12 workshops. Both workshop facilities were multi-product and were not dedicated. The manufacturing areas were of a good standard and suitable for the activities conducted therein. The exposed surfaces were smooth, impervious and unbroken to minimize the shedding or accumulation of particles or microorganisms and permitted the repeated application of cleaning. The classified areas were manually monitored for temperature, relative humidity, and pressure differentials. No BMS system for environmental control was in place.

QC laboratories

The laboratory areas and operations were separated from production areas. The physical-chemical, instrumental and microbiological laboratories were well organized and maintained in current state of art. T/RH were checked and recorded. The microbiological laboratory was separated from chemical laboratory. Separate entrances via changing rooms were provided to positive control room and microbial limit testing room.

Purified Water (PW) system, Workshop No 12

Three phases validation of the PW system was performed. The water was in continuous circulation at ambient temperature. Sanitization was performed upon in house schedule. The SOP "Monitoring of water for pharmaceutical use" and sampling plan for 2023 were checked and discussed. The PW system was seen to be clean and in good order.

HVAC system

AHUs were providing air to workshop clean rooms. The filter cascade was following primary filter → secondary filter → HEPA. The pressure differentials between primary and secondary filter were monitored on-line. Sound and light alarm systems were provided. Each AHU had PLC for monitoring T/RH in critical production rooms and pressure differential between corridor and atmosphere.

AHU's IQ, OQ and PQ were performed following the SOP "Monitoring of clean area". The testing schedule was defined in the SOP "Monitoring of air cleanliness in clean area". The HVAC system was seen to be clean and well maintained.

Nitrogen system

Nitrogen was used in the manufacturing process. The P & ID, sampling point of nitrogen and the SOP "Specifications and test method for Nitrogen "were checked. The sampling and testing schedule was performed according to the in-house procedure.

5. Process equipment

Design and construction

The equipment used in the manufacture of Levofloxacin appeared to be of appropriate design and size for its intended use. The manufacture and material transfer took place in closed systems wherever possible.

The equipment installed in the inspected production workshops were multi-purpose and each piece of equipment had a unique identification number.

Equipment maintenance and cleaning

The equipment viewed during the inspection appeared suitably maintained and in good condition. Equipment status labels were available. Written procedures were established for equipment preventive maintenance. Food-grade oil as lubricant was used.

In general, the production equipment was well maintained, and equipment were free of dust and residues. Calibration and maintenance schedules for laboratory equipment/instruments and production equipment/instruments were available and presented to the inspectors. Spot checks showed that schedules were followed.

6. Documentation and records

The 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 with maintenance of revision histories. A procedure was established for retaining documents. Retention periods for documents of QMS, production, quality control, and distribution records were specified.

The 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 respective activity.

The laboratory control records included complete data derived from all conducted tests to ensure compliance with established specifications and standards.

The batch numbering system and BMR management were following SOP "Batch numbering system" and SOP "Record release, QC record compile, check, print, storage and dispense" respectively. The Levofloxacin API codes were defined following SOP "Finished products numbering". The master BMR for WHO Levofloxacin API was checked and discussed.

7. Materials management

The incoming starting materials and finished API products were quarantined after receipt until being released for use or distribution. The status of raw material was indicated, with respect to the material under quarantine, approved, and retest, etc. The starting material, packaging material and finished API products were stored in different warehouses under the specified conditions. A secured area for return and rejected materials were in place. The starting material and finished goods were managed by a manual system. The warehouses for starting materials were visited during the inspection. The management procedures for material receiving, sampling, testing and release were checked,

Vendor audit

A system for evaluating the suppliers of critical materials was in place. The SOP "Supplier quality audit" and the 2023 annual plan for site audit of suppliers, including contract labs were available. The audit report to an intermediate supplier was checked.

8. Production and in-process controls

Production of Levofloxacin took place in Workshops No.11 and No.12. All the production areas were visited and found to be of suitable standard generally, clean and logically organized to suit their intended purpose.

In-process sampling and controls

In-process sampling was performed at defined stages during processing.

Contamination control

The API purification, crystallization and drying were performed using non-dedicated equipment in the clean area of production block. SOP "Prevention of contamination and cross-contamination" was checked and appeared acceptable.

9. Packaging and identification labelling of APIs and intermediates

The packaging materials and labels were subjected to quality control before release. The packaging and labelling processes were in operation at the time of the inspection. The packaging and labelling operations were described in the batch packaging instructions. The line clearance was checked and showed it was done before and after labelling/packaging procedures.

10. Storage and distribution

Warehousing procedures

The finished APIs were stored in a designated warehouse and held until released by the Authorized Person. Facilities were available for the storage of materials under appropriate conditions. Records were maintained of these conditions. Separate storage areas were provided for quarantine, rejected, returned or recalled materials.

The temperature mapping procedure SOP "Temperature mapping management" was checked. The worst-case location should be identified for routine monitoring.

Distribution procedures
The APIs and intermediates were released for distribution to third parties after they have been released by the quality unit and transported in a manner that did not adversely affect their quality. 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.

11. Laboratory controls
Adequate quality control facilities were provided. Procedures were in place describing sampling, testing, approval or rejection of materials and recording and storage of laboratory data. Specifications, sampling plans and test procedures were available.

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.

Sample receiving and distribution
Finished API samples were collected by QA personnel. Samples receiving/storage/distribution records were maintained, samples were appropriately stored.

Testing of intermediates and APIs
Analytical raw data report for Levofloxacin was briefly checked. Validated excel sheets were used to calculate assay and related substances. Analytical raw data reports were reviewed by the QC manager or supervisor.

The SOP "Certificate of Analysis for distribution use" was checked. The data to the CoA was entered by Quality Unit QA and approved by Head of quality management (QP) or Head of Quality Unit and head of QA.

OOS/OOT management
OOS/OOT was managed according to the SOP "OOS/OOT handling" and the SOP "Microbiological OOS handling". The procedure, OOS flow chart and following OOS were reviewed and discussed.

Retention samples
The SOP "Retention sample" was checked. A retention sample register was in place. Reserve samples of each batch of API were retained. The retention samples of key starting material and intermediate were also kept. The room condition was controlled upon SOP "Temperature and humidity controlling of quality testing room".

Stability study
A range of stability chambers were available. Stability monitoring programme followed the SOP "Stability test". The chamber's calibration was performed yearly.

Laboratory equipment
All laboratory equipment had usage and calibration logbooks. HLPC columns were stored in good order, and usage look books were available. The pH, analytical balances and Karl Fisher titrator calibration/verification were performed. Class "A" volumetric glassware was used.

12. Validation

Validation and qualification were described in the Validation Master Plan (VMP) and management system procedure for production process validation. Process validation was required to be either prospective or concurrent. Periodic validation was performed as required by the inhouse procedure.

Validation documentation

The validation protocols for Levofloxacin API and a validation report had been prepared with results compared to acceptance criteria with a documented conclusion. The PV protocol and report for Levofloxacin API with three PV batches were checked and found acceptable generally.

Qualification

Qualification of key equipment was a prerequisite for process validation. Qualification protocols and reports were available for key equipment. These were cross-referenced in the process validation documentation.

Cleaning validation:

The SOP, cleaning validation protocol and report for Levofloxacin were available. The SOP "Equipment cleaning validation" and cleaning validation performed with three PV batches were checked. The lowest residue limit was defined. Both rinse and swab method were applied, and result was within the limit. The clean and dirty holding time were also validated. The analytical method validation for residue material in cleaning validation was briefly checked and appeared acceptable.

Equipment qualification

Appropriate qualification of critical equipment and ancillary systems were performed in accordance with the SOP "Equipment qualification". It also described periodic requalification for equipment. The PQ reports on tanks used in Levofloxacin production were checked.

Computerized system validation

Computerized systems were not used for material or production control. A computerized system was used in QC lab for HPLC and GC networking. GMP-related computerized systems in QC lab were validated. The relevant documents were available and checked.

13. Change control (CC)

A change control system was established. The SOP "Change control" and the flow chart were checked. Potential impact of the proposed change on the quality of the intermediate or API was evaluated. Measures were taken to ensure that documents affected by the changes were revised. The CC registers for 2022 and 2023 were checked. Several change controls were reviewed.

Deviations

Deviations were managed according to the SOP "Deviation handling". Deviations were classified as: Minor, Major and Critical. Trending of deviations was performed annually. The deviation regarding Levofloxacin hemihydrate production control was checked and discussed.

CAPA

The SOP "Corrective and preventive action management" was checked. The QA was responsible for follow-up and implementation of CAPAs. CAPAs logbooks for 2023 and 2022 were checked. Logbooks specified expected completion and actual completion dates.

14. Rejection and re-use of materials

The SOP "Reprocessing and reworking" was checked. In case of re-processing – a request form was issued by the workshop manager and approved by the Quality department. The issuance of the re-processing form was controlled by QA. According to the company, no batch was reprocessed in last three (3) years. Re-working was not allowed.

The SOP "Receipt, storage, distribution and return of materials" was checked. Returned intermediates or APIs were identified and quarantined in returned goods storage room and checked by the warehouse/QA and sales personnel. The Returned products register for 2022 was checked.

The SOP "Solvent recovery" was checked. According to the SOP, recovered solvents could be used in the same processing step or the same product previous processing steps. The solvent recovered and used in Levofloxacin production was checked.

15. Complaints and recalls

Quality-related complaints were recorded and investigated according to a written procedure. The records of complaints were retained.

The SOP "Customer complaint and recall procedure" was checked. Complaints could be received by sales or by other departments and reported to QA department. QA was responsible to record the complaint and organize investigation by respective departments. The QA manager or Quality Unit manager were responsible for classification of complaints. If necessary, complaint investigation could lead to product recall. Complaints register for 2022 and 2023 as well as the complaints investigations were checked.

The Product recalls were classified into three classes. The classification was according to health impact and urgency. The Head of Quality Management was responsible for making decision regarding recall. Until the date of inspection, no recalls were recorded for Levofloxacin API. Mock recalls were performed at specified time intervals.

16. Contract manufacturers (including laboratories)

There was no contract manufacturing of Levofloxacin API. An external contracted laboratory was used for genotoxic impurity testing. The vendor audit report was checked and discussed.

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, **Zhejiang East-Asia Pharmaceutical Co., Ltd.,** located at **Coastal Industrial City, Pubagang town, Sanmen County, Zhejiang, P.R. China** was considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

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

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

Part 4	List of 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-eight Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO TRS No. 986, Annex 2***
   https://digicollections.net/medicinedocs/documents/s21467en/s21467en.pdf

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***
   untitled (digicollections.net)

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
   9789240020900-eng.pdf (who.int)

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
   https://digicollections.net/medicinedocs/documents/s21440en/s21440en.pdf

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**
   https://digicollections.net/medicinedocs/documents/s23455en/s23455en.pdf

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. 961, 957), Annex 1
   https://digicollections.net/medicinedocs/documents/s18681en/s18681en.pdf

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
   https://digicollections.net/medicinedocs/documents/s22358en/s22358en.pdf

8. 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
   TRS 1044 - Annex 2: WHO good manufacturing practices for sterile pharmaceutical products

9. WHO guidelines on technology transfer in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Sixth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 1044), Annex 4.
   Short name: WHO TRS No. 1044, Annex 4
   TRS 1044 - Annex 4: WHO guidelines on technology transfer in pharmaceutical manufacturing

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***
    https://digicollections.net/medicinedocs/documents/s18683en/s18683en.pdf

11. 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***
    https://digicollections.net/medicinedocs/#d/s21438en

12. 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
    https://digicollections.net/medicinedocs/documents/s18682en/s18682en.pdf

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
    https://digicollections.net/medicinedocs/#d/s20177en/

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
    https://digicollections.net/medicinedocs/#d/s20175en/

15. 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

16. 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***
https://digicollections.net/medicinedocs/documents/s23697en/s23697en.pdf

17. 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

18. 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***
Essential Medicines and Health Products Information Portal (digicollections.net)

19. WHO Recommendations for quality requirements when plant – derived artemisinin 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
https://www.who.int/publications/m/item/who-recommendations-for-quality-requirements-when-plant-derived-artemisinin-is-used-as-a-starting-material-in-the-production-of-antimalarial-active-pharmaceutical-ingredients---trs-992---annex-6

20. 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***
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21. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
Short name: WHO TRS No. 996, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

22. 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

23. 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**
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24. 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**
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25. 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**
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26. 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

27. 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***
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