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

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**Changzhou Yabang-QH Pharmachem Co., Ltd**
Corporate address of manufacturer	No.18 Jinlong Road, Chunjiang Town Changzhou City, Jiangsu P. R. China 213127
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Changzhou Yabang-QH Pharmachem Co. Ltd. No.18 Jinlong Road, Chunjiang Town Changzhou City, Jiangsu P. R. China
Synthetic unit /Block/ Workshop	Workshops 1, 2, 3, 5 Workshop 1 ([4-amino-3-nitrophenyl] phenylmethanone, Mebendazole starting material and Mebendazole API) Workshop 2 ([4-amino-3-nitrophenyl] phenylmethanone, Mebendazole starting material) Workshop 3 (Albendazole API, Mebendazole API) Workshop 5 (Methyl cyanamido formate, intermediate for Albendazole)
Inspection details	
Dates of inspection	20-22 January 2025
Type of inspection	Routine inspection
Introduction	
Brief description of the manufacturing activities	Changzhou Yabang-QH Pharmachem Co., Ltd. is authorized to manufacture intermediates and API's for animal and human use. The table below an overview of the APIs and intermediates currently manufactured in each workshop

Workshop	**Product**	**Human/Animal Use**
1	Mebendazole	Human/Animal
	Flubendazole	Human/Animal
	Closantel Sodium Dihydrate	Animal
	Diclazuril	Animal
	Febantel	Animal
	Oxyclozanide	Animal
	Oxfendazole	Animal

		Fluralaner	Animal
		Eprinomectin	Animal
		Oclacitinib maleate	Animal
		Oxibendazole	Animal
	2	Starting Materials and Intermediates related to APIs	Animal
	3	Mebendazole	Human/Animal
		Flubendazole	Human/Animal
		Albendazole	Human/Animal
		Closantel Sodium Dihydrate	Animal
		2-nitro-5-phenylthio aniline	Animal
		Trans-4-[(tert-butoxycarbonyl) amino] cyclohexanecarboxylic Acid (4-NBA)	Animal
		Levamisol Hydrochloride	Human/Animal
		4-Chloro-7H-pyrrolo[2,3-d]pyrimidine (4-CPP)	Animal
		Fenbendazole	Animal
		N-[8-(2-hydroxybenzoyl)amino]caprylate sodium (SNAC)	Human
	5	Starting Materials related to APIs	Human/Animal

General information about the company and site	Changzhou Yabang - QH Pharmachem Co., Ltd. was established in 2004. Most of its manufacturing facilities were constructed in 2004 and 2005, while workshop 3 was designed and constructed between 2007 and 2010. The site has four workshops, several warehouses, one utility building, one QC/R&D building and two administration buildings. The facilities are approximately located 28 kilometers from Changzhou.
History	This was the fourth WHO inspection. The previous WHO inspection was conducted in May 2019. The site undergoes regular inspections by national and local authorities. The most recent inspection was carried out by the Jiangsu Medical Products Administration in August 2024.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Pharmaceutical Quality System Personnel Documentation Facilities and Equipment Production Quality Control Packaging and labelling Product Release Purified Water System

Restrictions	
Out of scope	APIs and intermediates not submitted to WHO Prequalification were not included in the scope of this inspection.
WHO APIs covered by the inspection	Mebendazole Albendazole
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GMP	Good manufacturing practices
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high-performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IQ	Installation qualification
KF	Karl Fisher
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MR	Management review
NC	Non conformity
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system

PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
RO	Reverse osmosis
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer

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

The company had implemented a Quality Management System (QMS) based on ICH Q7, PIC/S, and EU GMP standards. The Quality Manual outlined the core principles of the system. It detailed the company's organizational structure, including the roles and responsibilities of employees at all levels, and described the processes for monitoring and continuously improving the QMS. The documentation system was structured into three levels: Level 1 (Quality Manual, SMF, Management Procedures), Level 2 (Operational Procedures), and Level 3 (Records). Personnel interviewed during the inspection had the necessary experience and training to support the manufacturing activities while facilities and equipment were qualified and well maintained.

Management Review

Management reviews were conducted quarterly, as outlined in a written SOP. During each meeting, key topics discussed included follow-up actions from the previous review, quality policy, product trend analysis, assessment of the Quality Management System, CAPA, complaints, returns, recalls, self-audits, supplier audits, APQR, changes, deviations, registrations, and VMP. Key Performance Indicators (KPIs) had been established to monitor performance. The minutes of the meeting held on 24.10.2024, covering the period from July to September 2024, were reviewed and discussed.

Data Integrity

A procedure for data integrity was established, covering all GMP-related documentation, including both electronic and paper-based records. The SOP referenced the principles of ALCOA and ALCOA+, outlining the requirements for maintaining data integrity. Separate guidelines and protocols were defined for ensuring the integrity of paper-based and electronic documentation. Additionally, a Data Integrity Risk Assessment was conducted to identify and mitigate potential risks.

Quality Risk Management

Quality Risk Management was applied to all GMP activities on-site, including R&D, with the foundational concepts outlined in a written procedure. The principles of ICH Q9 were thoroughly detailed in the SOP, which also described standard tools for risk assessment, with FMEA being the most commonly used. A matrix was employed to determine the appropriate risk assessment tool for each situation. The procedure included instructions for risk review, with clear triggers defined for when

reviews should take place. High-risk processes required re-evaluation every six months, medium-risk processes were reviewed annually, and low-risk processes were re-evaluated every two years.
The risk assessments for the formation of nitrosamines during the manufacturing processes of Albendazole and Mebendazole were discussed. Despite the presence of secondary amine groups in the raw materials and intermediates, the risk of nitrosamine formation was deemed low. It was recommended that the company conduct analytical testing for nitrosamine detection during the next cleaning validation/verification exercise.

Deviations
A procedure for handling deviations was in place and was thoroughly discussed. Deviations were classified as either critical or non-critical. A designated team was responsible for conducting root-cause investigations. Deviations were reviewed quarterly and compiled into an annual report. The deviation trend report for the period April to July 2024 was reviewed. The QA department maintained a register of all deviations. Examples of deviation handling were reviewed.

2. Personnel
There were approximately 300 members of staff working on site. Key personnel responsibilities were described in job descriptions and the hierarchical and administrative structure was depicted in the organization chart.

3. Buildings and facilities
The campus comprised several buildings and workshops (1, 2, 3, and 5). WHO-approved APIs, Mebendazole and Albendazole, were produced in Workshop 3, with Workshop 1 serving as a backup for Mebendazole production. (4-amino-3-nitrophenyl) phenylmethanone, a key starting material for Mebendazole, was manufactured in Workshop 2. Methyl cyanamido formate, an intermediate for Albendazole, was produced in Workshop 5. The campus also housed dedicated warehouses, the QC/R&D building, the Utilities Unit, and the PW system Unit. Layouts of the facilities were provided. Generally, the premises were constructed, designed, and maintained to fit the operations conducted and prevent contamination risks of materials and products. Overall, the design of the premises aimed to minimize errors and allow for effective cleaning and maintenance

4. Process equipment
In general, the production equipment met the required standards. Reactors, centrifuges, microfilters, press filters, dryers, mills, sieves, mixers, and utilities were installed to support the mixing, heating, cooling, crystallization, centrifugation, drying, and milling processes necessary for the production of the APIs. Pipelines were clearly marked, and utensils, tools, and equipment were uniquely identified, with status labels applied accordingly. Measuring equipment was also labelled with calibration status and maintained in accordance with written procedures. A preventive maintenance plan was in place, and records of all maintenance activities were kept.
The equipment was installed in a logical order to optimize production flow while minimizing the risk of contamination and mix-ups. An SOP on cross-contamination management was established and reviewed.
A procedure for managing utensils and production tools was presented. It outlined the handling of centrifuge bags during manufacturing campaigns. Centrifuge bags used in preliminary synthetic steps were not cleaned between batches during campaign manufacturing. However, centrifuge bags were cleaned after every batch during the final processing steps in the clean area. Maintenance records for

centrifuges in Workshop 1 were reviewed, with controls performed every 15 days, 3 months, 6 months, and annually.

5. Documentation and records

Most of the QMS documentation was in Chinese. It is recommended that key QMS procedures be translated into English to facilitate future GMP inspections.

A procedure for issuing SOPs was established to standardize the process for issuing, revising, reviewing, and numbering SOPs. The relevant department or system owner was responsible for drafting the documents, while the department manager or QA was tasked with reviewing them. Ultimately, the QA manager or the Quality director was responsible for approving the documents. Documentation management followed the Document Control Management procedure and the Record Management procedure. The QA department printed and stamped records for the various departments, and the serial number of each page was logged in a logbook.

Batch numbering system

A procedure defining the codification and issuance of batch numbers was in place.

6. Materials management

Starting materials, packaging materials, intermediates, solvents, and finished products were stored in dedicated warehouses. The raw material warehouse in Building E was visited on the first day of the inspection. Established procedures were in place for the receipt, quarantine, sampling, release, and storage of raw and packaging materials. Material receipt was performed using a checklist. Temperature and relative humidity were consistently monitored and recorded at the warehouses. A list of approved suppliers was also maintained. Incoming materials were placed in designated areas or marked with status labels: yellow for quarantine, green for release, white for sampling, and red for rejected materials. The issue of quarantine labels was recorded in a logbook. Packaging material was stored on the first floor of the finished product warehouse in Building D. Sampling on primary packaging material was conducted based on $\sqrt{n}+1$ method in the microbiological laboratory. Liquid solvents in drums were stored in Building 2A. A sampling room for solvents in drums was established in the warehouse.

A tank farm was established to house tanks for Toluene, Methanol, NaOH, Formic Acid, Acetone, Isopropanol, and Butanol. Before unloading, the tanker and solvent documentation were checked. Bulk solvents were sampled and tested, with results considered before transferring the solvent into the tank via dedicated flexible hoses. After mixing with the existing solvent in the tank, a new sample was withdrawn and analysed. A new batch number was assigned following positive test results. Documentation related to Methanol batch: H2501019 was reviewed.

Additionally, the SOP for the maintenance of storage tanks and the maintenance logbook for the NaOH solution storage tank were reviewed.

7. Production and in-process controls

In general, production operations followed defined procedures. Process flows and routes of synthesis were made available.

On the first day of the inspection, Workshop 3 was visited. The workshop consisted of three floor. The second floor housed the reactor area and the dispensing room. Raw materials were lifted to the second floor, checked in the staging area and registered in the production logbook, before dispensing. A spot check was performed on the logbook the received quantities were recorded. The scoops used for dispensing were dedicated to each material. They were kept in a plastic container bearing a cleaned status label and the validity date. A clean hold time study was available to support the 7-day duration

during which utensils maintained their clean status. The dispensing room's usage logbook and the daily calibration logbook for a dispensing balance were also spot-checked. For solvents in drums, dispensing took place in production and was performed by weight. At the time of the inspection, the first stage of a Mebendazole batch was in progress. The corresponding BMR and usage logbook for the reactor were reviewed. Mebendazole was manufactured in campaign.

Centrifuges were installed on the first floor of the workshop. Centrifuge bags were visually checked for integrity at batch change over and this was recorded. They were stored in a dedicated room and were discarded after each campaign, with this being recorded in a logbook.

Two dryers were in use on the ground floor. The BMR of a Mebendazole batch was reviewed during the drying stage (Stage 2: crude product). Crude Mebendazole after treatment with activated charcoal and filtration was transferred to the clean area and dissolved in formic acid.

The final processing steps—purification, crystallization, centrifugation, drying, milling/sieving, homogenization, and packaging—took place in the Clean area (Grade D) located on the ground floor of the workshop. The BMR of a Mebendazole batch in Stage 3 including the dilution and crystallization processes were checked in detail.

There has been no production of Mebendazole API for WHO since the last WHO inspection (May 2019).

Workshop 5 was visited on the second day of the inspection. Methyl cyanamido formate, an intermediate for Albendazole API, was produced on the first floor of this workshop. Packaging of the intermediate took place on the ground floor.

Workshop 1 was also visited. This workshop was used as a back up to produce Mebendazole. In addition, (4-amino-3-nitrophenyl) phenylmethanone, a starting material for Mebendazole was also produced. The building consisted of two floors. The reactor area was housed on the first floor while centrifugation took place on the ground floor. A Grade D area dedicated to the final processing steps was also found on the ground floor. Access to this area was restricted and dedicated entry was available.

8. Packaging and identification labelling of APIs and intermediates

Packaging material was stored on the first floor of the finished product warehouse (building D). Primary packaging took place in the Grade D area. The API was packed in double LDPE bags and finally in fiber drums. The labels were generated by QA. Tamper proof seals were placed on the carton containers.

9. Storage and distribution

After packaging, the APIs were stored in Warehouse D. The QC department tested the batch against approved specifications and submitted data to the QA department for review. Once all documents confirmed conformance, the QA department released the batch for distribution. The API's quality status was changed from yellow (quarantine) to green (release), and the identification label on each drum was stamped as released.

10. Laboratory controls

The QC laboratory was found in a separate building. The ground floor housed the physicochemical laboratory including the wet chemistry room, the UV room, the HPLC room, the GC room, and the stability studies room. The microbiological laboratory, the retained samples room and the particle size determination laboratory were found on the first floor. The second floor housed the R&D centre. Quality Control (QC) operations were independent of production. The QC laboratories were appropriately designed and equipped with the necessary physicochemical and microbiological testing

equipment, including but not limited to HPLC, GC, balances, pH meters, conductivity testers, IR and UV spectrophotometers, melting point apparatus, TOC analysers, and potentiometric titrators.
There were SOPs in place for sampling and sample management and testing. A list with the quantities to be sampled for each raw material was presented. Amber vials were used for collecting samples of finished products and light-sensitive raw materials, while small HDPE bags were used for other solid raw materials. Spot checks were conducted on equipment use and calibration logbooks. The procedure for using the pH meter and the procedure for preparing pH standard solutions (were presented and discussed.
Furthermore, the working instructions for the IR ThermoScientific were reviewed. The IR spectrum of a Mebendazole batch was spot-checked.
In addition, the procedure for data integration in HPLC and GC was presented. Manual integration was not normally allowed. If manual integration had to be performed it was handled as a deviation and it was assessed and approved by QA. Only the QC Administrator had privileges to perform manual integration. The SOP on Electronic Data Management Procedure in the QC laboratory was reviewed. A trained analyst conducted an audit trail review for each sequence. QA was responsible for reviewing the audit trail on a weekly basis, and the QC Supervisor conducted monthly reviews. The audit trail review records conducted by QA on 08.12.2024 and by the QC Supervisor in November 2024 were spot-checked.
Moreover, during the visit to the analytical laboratory the following documentation was reviewed:

- The STP for Mebendazole API
- The Mebendazole API batch: 65425004 analytical raw data including related substances by HPLC, and the audit trail.
- The Mebendazole reference standard usage log, and reconciliation sheet.
- The STP for Albendazole API
- The Albendazole API batch 68322001 analytical raw data including related substances by HPLC, and the audit trail
- The Albendazole reference standard usage log, and assay determination by titration.
- The Mebendazole API batch 65424153 residues analysis in GC including the audit trail.
- The SOP on Handling of reagents

Reference standards

The laboratory maintained a list of reference standards including the lot numbers, the quantity of each vial and the storage conditions. In addition, another logbook was used for managing the inventory of reference standards. A procedure for handling of reference/working standards was spot checked. The validity of reference standards was checked monthly.
The inventory and the CoAs of Mebendazole CRS and Albendazole CRS were checked.

OOS Handling

A procedure for handling OOS/OOT results was in place and briefly discussed. Phase IA verified any obvious errors whereas Phase IB covered the verification of analyst, method, and reagent before hypothesis testing was performed. If no laboratory error was detected, phase II started in manufacturing process. A review of OOS was included in APQR of each product.

Stability Studies

Eight stability chambers were installed, with five in operation to cover all ICH climatic conditions. For each batch undergoing stability studies, a protocol was available that outlined the stability conditions, the number of samples, the time points for sample withdrawal, and the quantity to be withdrawn at

each time point. A procedure was in place for determining the acceptable time tolerance for sample withdrawals relative to the target date. Testing of withdrawn samples had to be completed within 14 days from withdrawal.

The stability studies for Albendazole validation batches were reviewed under accelerated conditions. The stability study parameters included appearance, total impurities, impurity A, impurities B & C, impurity D, impurity E, impurity F, impurity H, melting point, LOD, and assay. Additionally, the stability studies for these batches at 30±2ºC/75±5%RH were reviewed and discussed. Stability data for up to 24 months was made available, and the analytical record for the 24th-month time point at 30±2ºC/75±5%RH for one of the batches was reviewed in detail.

11. Validation

There was a procedure in place describing the principles of establishing the VMP and providing an overview of the validation operations, activities, organizational structure, and planning. The VMP was revised annually, and the scope included qualification/validation activities to be carried out regarding facilities, equipment, instruments, manufacturing processes, analytical methods, cleaning validation and computerized systems. The requalification frequency of the equipment was every 5 years, and 3 years for instruments. The following schedules describing validation activities at different GMP areas were available and were checked:

- 16.01.2025 for equipment.
- 16.01.2025 for processes
- 16.01.2025 for methods
- 16.01.2025 for cleaning
- 16.01.2025 for Computerized Systems

The protocol and report for the process validation of Albendazole were reviewed. The process validation was initiated through a series of change controls due to a change in the test method for particle size and for primary packaging as well as the introduction of new suppliers and a change in residual solvent specifications. Three batches were manufactured. Roles and responsibilities for involved departments were defined. Product specifications were set according to the Ph.Eur. monograph.

Cleaning validation

There was a procedure in place for cleaning validation. Cleaning methodologies were adequately described. Similarly swab, rinse and reflux sampling processes were detailed. The acceptance criteria were based on PDE, NOEL or on concentration NMT 20 ppm. The following documents were reviewed:

- The cleaning validation report. An evaluation was conducted to include the tools used in production and dispensing. Additionally, an evaluation study was performed due to the introduction of Albendazole API. The final cleaning validation report also reviewed.
- The Matrix of multipurpose equipment used in the chemical and clean areas of workshop 3.
- The PDE determination for Mebendazole was provided. The PDE determination for Closantel was also provided. The customer was responsible for providing the PDE determination. Toxicological reports and PDEs for the same API were submitted by several customers, and the company adopted the most stringent PDE value. Additionally, since the equipment was commonly used for producing APIs for veterinary purposes, PDE values for APIs intended solely for veterinary use, without any further toxicological assessment, were utilized in the calculations of MACO.

12. Change control

A procedure for managing changes was in place. The scope covered all GMP areas affecting product quality including but not limited to materials, facilities, equipment, processes, specifications, analytical methods, and quality documentation. Changes were categorized in major or minor and temporary or permanent. The user was responsible for the initiation of a change. The head of the department/designee was responsible for the initial review, and assessment. The QA department reviewed the change and forwarded to the concerned department. For major changes a risk assessment was mandatory.
The change control log of Mebendazole, for 2019-2024 and Albendazole for 2022-2024 was presented. Examples of changes were reviewed in detail.

13. Rejection and re-use of materials

A procedure for reprocessing and reworking was presented and discussed in detail. Specific instructions for reprocessing and reworking were available for both intermediates and finished products. If an intermediate or finished product was found to be out of specification, a deviation was raised, and an investigation was conducted. The root cause investigation had to be completed before any proposal for reworking or reprocessing could be made. Proposals for reworking or reprocessing typically came from the technical team (R&D or Production) and were incorporated into the CAPA process.
Reworking followed the change control procedure, although the new process was applied only once, with no intention to continue its use, and process validation was not considered. Reworked batches were placed under both accelerated and long-term stability studies and were not released until the accelerated study was completed. The customer had to be informed of any reworking. A similar approach applied to reprocessed batches, but in this case, the batch was released once finished product testing was completed, and the customer was not informed according to the standard quality agreement.

Solvent recovery

A procedure for solvent recovery was presented. Specifications for fresh Ethanol and recovered Ethanol were established but were not equivalent. The water content in recovered Ethanol was up to 50%. As part of the initial process validation the third batch was manufactured only using recovered ethanol. Additionally, the company presented a study where recovered Ethanol was used for 20 consecutive batches and the test results were according to specifications.

14. Complaints and recalls

There was a procedure in place for handling complaints. The QA department was responsible for logging, recording, classifying, and investigating the complaint. The complaint investigation report included root cause and CAPAs. An annual review was conducted, and records were kept for 12 years. Example of complaint handling and relevant root cause investigations were reviewed.

The procedure for recall was presented. Recalls were categorized into three classes (I, II, III) based on health impact and urgency, with class I being the most critical and urgent. Responsibilities and timelines for conducting investigations and taking the recall decision were established (24h for Class-I, 48h for Class-II and 72h for Class-III). The product recall committee was responsible for coordinating product recalls. A mock recall was carried out every 2 years unless a recall was carried out in the previous year. No recall had been carried out. Documentation relating to the last mock recall performed in 11.2023 for Mebendazole batches was reviewed.

15. Contract manufacturers (including laboratories)

None of the production processes related to the manufacturing of the WHO APIs were contracted out. Similarly, analytical testing related to WHO APIs was not contracted out.

Part 3	Conclusion – Inspection outcome

Based on the areas inspected, the people met, and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, ***Changzhou Yabang-QH Pharmachem Co., Ltd, located at No.18 Jinlong Road, Chunjiang Town, Changzhou City, Jiangsu, P. R. China*** as considered to be operating at an acceptable level of compliance with WHO GMP Guidelines for APIs.

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

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

Part 4	List of GMP Guidelines referenced in the inspection report

1. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2. ***Short name: WHO TRS No. 957, Annex 2***

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 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

4. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4.
   Short name: WHO TRS No. 937, Annex 4

5. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-first Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. ***Short name: WHO TRS No. 943, Annex 3***

6. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-seventh Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052, Annex 4).
   Short name: WHO TRS No. 1052, Annex 4

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

8. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 6.
   Short name: WHO TRS No. 961, Annex 6

9. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7.
   Short name: WHO TRS No. 961, Annex 7

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**

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 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***

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***

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***

15. WHO Guidelines on good manufacturing practices: validation, Appendix 7: non-sterile process validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 3. ***Short name: WHO TRS No. 992, Annex 3***

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 general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
Short name: WHO Multisource guidance or ***WHO TRS No. 996, Annex 10***

19. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8. **Short name: WHO TRS No. 1010, Annex 8**

20. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 10.
Short name: WHO TRS No. 1010, Annex 10

21. Production of water for injection by means other than distillation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 3.
Short name: WHO TRS No. 1025, Annex 3

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

23. 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

24. Points to consider when including Health-Based Exposure Limits (HBELs) 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 1033, Annex 2

25. 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 1033, Annex 3***

26. 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 1033, Annex 4***