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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	**Hebei Xingang Pharmaceutical Co Ltd**
Corporate address of manufacturer	No.2 Fuqiang Street, Zhaoyuan Road, Zhao County Shijiazhuang, Hebei 051 530 P. R. China
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Hebei Xingang Pharmaceutical Co Ltd Site A(Site-East): No.82 Zhaoyuan Road, Zhao County, Shijiazhuang Longitude:114º44'18.72", Latitude: 37º45'29.66" Site B (Site-West): No.2 Fuqiang Street, Zhaoyuan Road, Zhao County, Shijiazhuang Longitude:114º43'40.44", Latitude: 37º45'38.52"
Synthetic unit /Block/ Workshop	Site A(Site-East): No.82 Zhaoyuan Road, Zhao County, Shijiazhuang (for the fermentation and extraction processes of Rifamycin-S-Na) Site B (Site-West): No.2 Fuqiang Street, Zhaoyuan Road, Zhao County, Shijiazhuang (for the synthesis of Rifampicin, Quality Control activities and warehousing)
Inspection details	
Dates of inspection	14-17 January 2025
Type of inspection	Initial inspection
Introduction	
Brief description of the manufacturing activities	The manufacturing authorization covers activities and operations taking place in the Site-West where Rifampicin and Rifandin are manufactured. Manufacturing activities related to Rifamycin fermentation processes (i.e., Rifamycin-S and Rifamycin-S-Na) conducted in Site-East are not covered by the license.

General information about the company and site	Hebei Xingang Pharmaceutical Co., Ltd. was founded in 1998 and is located at the Light and Textile Industries Zone in Zhao County, Shijiazhuang, Hebei Province, approximately 50 km from Shijiazhuang city and the airport. The company consists of two sites (Site-East and Site-West), which are located within 1 km of each other. The company's official registered address is No. 2 Fuqiang Street, Zhaoyuan Road, Zhao County, Shijiazhuang City, Hebei Province, P.R. China where Site-West is located. Rifamycin S-Na is manufactured at Site-East, while Site-West is responsible for the production of Rifampicin API.
History	This was the first WHO PQ inspection.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Pharmaceutical Quality System Documentation Facilities and Equipment (Site-East and Site-West) Purified Water System Production Quality Control Packaging and labelling Product Release
Restrictions	N/A
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	Rifampicin (Polymorph II) Rifampicin (Polymorph I)
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis

GMP	Good manufacturing practices
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high-performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IQ	Installation qualification
KF	Karl Fisher
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MR	Management review
NC	Non conformity
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
RO	Reverse osmosis
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer

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

1. Quality management

The company had established a QMS that was applicable to all manufacturing operations on-site. The Quality department was independent of the Production department. Operations were specified in written form and critical GMP requirements were being met. The procedures reviewed and discussed during the inspection were generally of an acceptable standard. The Quality department was responsible among others, for the release or the rejection of APIs, intermediates and raw materials, the review of BMRs, the investigation for any major deviations, self-audits, approval of changes, and PQRs.

Management Review

Management review was performed annually and described in a written procedure. During the meeting, among others the following were discussed: follow up actions from previous management review, changes, deviations, OOS, CAPAs, audits, complaints, improvements, product quality, resources, goals. The minutes of the most recent meeting covering the period January to December 2024 were reviewed.

Product Quality Review

PQRs were conducted annually including batches manufactured between January and December according to a written procedure. The Rifampicin PQR had to be completed by the end of February for batches manufactured from January to December the previous year. One report was generated since the same raw materials and suppliers were used. However, the finished product batches were evaluated in groups depending on the finished product specifications. The PQR included batches that have been completed and tested but not necessarily released since release was performed when the batch was ready to be shipped to a specific customer. Statistical analysis was performed using UCL and LCL.

- The 2023 Rifamycin-S-Na PQR was reviewed in detail.
- The 2023 Rifampicin PQR was also discussed.

No batches according to WHO specifications were manufactured since the API was not prequalified at the time of inspection.

Batch Release

Batch release took place according to a written procedure. The Qualified Person of the QA department was tasked for performing batch release. Batch certification was performed after final packaging and labelling. For international markets the labels were generated by QA and the labelling was conducted in the quarantine area. A review of the BMR, BPR and analytical record was performed before releasing the batch.

Deviations

A procedure for handling deviations was in place and was discussed in detail. Deviations were categorized as critical, major, or minor. Deviations were checked for recurrence, but no periodic review was conducted. A review was done in the APQR of each product. From the list of deviations for 2023-2025, several deviations were reviewed in detail.

2. Personnel

There were approximately 80 members of staff working at Site-East and 90 at Site-West with each individual dedicated to their respective site. Key personnel responsibilities were outlined in job descriptions, and the organizational structure, including both hierarchical and administrative details, was depicted in an organizational chart. The Qualified Person's job description was checked.

A procedure for training personnel was presented. The procedure described induction training, change in position training, annual training, and external training

3. Buildings and facilities

The Site-East consisted of the fermentation workshop, the extraction workshop, the raw material warehouse, a QC laboratory and a utilities area. Pest control measures were in place. Storage conditions at the raw material warehouse were determined. A sampling room was established in the raw material warehouse. The logbook of the sampling room was spot-checked.
The Site-West included the synthesis workshop, several dedicated warehouses (hazardous material, raw material, solvent in drums, packaging material, quarantine, finished product, Rifamycin-S-Na), the DMF recovery unit, an underground tank farm, and a newly commissioned Quality Control Center. The solid raw material warehouse included a sampling room and a rejected material room. Packaging materials were stored in a separate warehouse and sampling of primary packaging material was performed in the packaging area. Temperature limits for each one of the warehouses at Site-West were established. Layouts of the facilities were made available.

4. Process equipment

In general, production equipment was of appropriate standard. Reaction vessels, centrifuges, double cone rotary vacuum dryers, vibration sieves, 2-D mixers, and utilities, were installed to allow mixing, heating, cooling, crystallization, centrifugation, drying, and milling required to make the API of interest. Pipelines were appropriately marked. Normally, utensils, tools and equipment were uniquely identified, and status labels were used. Similarly measuring equipment were labelled including the calibration status and, they were maintained according to written procedures. A plan for preventive maintenance was available and records of preventive maintenance were kept. The equipment appeared to be installed in a logical order to facilitate production and reduce the risk of contamination and mix ups. Procedures for the set up and operation of production equipment were made available.
The calibration of the thermohydrometer of the Rifamycin-S-Na warehouse was checked. The calibration was performed by an external service provider.

5. Documentation and records

All QMS related documentation was in Chinese. It is recommended that key QMS procedures (i.e. PQR, deviations, change control, complaints, recalls, OOS results, batch release) are translated to English to facilitate future inspections.

A procedure for issuing batch numbers was presented and discussed. According to the SOP, reworking was not permitted. Reprocessed batches were assigned a batch number ending with the letter "R." The remaining digits for the finished product batch number represented: "05" for Polymorph I, "07" for Polymorph II, one letter for grade/market (e.g., "W" for WHO), two digits for the year, two digits for the month, one digit for the production line, and a two-digit serial number for the month.

A procedure for determining the production date and the expiry date for a batch was in place. The production date was defined as the date the material was charged to the reactor. The expiry date was determined based on stability data and was calculated considering the manufacturing date.

6. Materials management Starting materials, packaging materials, intermediates, and finished products were stored in dedicated warehouses at Site-East and Site-West. Established processes were in place for the receipt, quarantine, sampling, release, and storage of raw and packaging materials. Receipt of materials was performed based on a check list. Temperature and relative humidity were consistently monitored and recorded. A list of approved suppliers was also maintained.

An underground tank farm was established, housing tanks for DMF, Acetone, Butanol, and Ethyl Acetate. Delivery documentation was reviewed, and sampling and testing were conducted before solvents were transferred to their dedicated tanks.

Sampling of primary packaging material (LDPE bags) adhered to the national standard (AQL) for the required number of bags to be tested. An SOP was available for reference.

7. Production and in-process controls On the first day of the inspection, the warehouse and fermentation workshop at Site-East were visited. The storage and inventory management of fermentation media, along with the relevant procedures on Reagents and Management procedure, Handling of Seed and Inoculation were thoroughly reviewed and discussed. Examples of records of inoculation were spot-checked. The material and personnel flow from the non-controlled area to the Grade C area were reviewed, along with the operation and loading processes of the Autoclave.

On the second day, the inspectors visited Site-West, where they examined the raw material warehouse, packaging material warehouse, Rifamycin-S-Na dedicated warehouse, and the tank farm. The inspectors also observed the material flow and manufacturing processes for Rifampicin. A temporary storage area for raw materials was set up in the synthesis workshop, raw material was hoisted to the mezzanine. Dispensing took place in the synthesis workshop after checking the raw materials. The usage logbook of the dispensing room and the logbook of daily calibration of balance were reviewed. Spot checks were performed on BMRs, as well as on equipment cleaning and maintenance procedures. The production of Polymorph I and Polymorph II took place in different areas of the same building. At the time of the inspection, manufacturing was in progress in the cyclization reactor. The relevant BMR and usage logbook of the reactor were spot-checked. Moreover, the BMR of the batch at the third stage of production was also presented. The final processing steps (purification, crystallization, centrifugation, drying, milling/sieving, and packaging) took place in a Grade D area located on the ground floor of the synthesis workshop.

8. Packaging and identification labelling of APIs and intermediates
Primary packaging took place in the Grade D area. The API was packed in an inner layer of LDPE bag and an outer layer of aluminum foil bag, purged with Nitrogen and finally placed in a fiber drum. For international markets the labels were generated by QA and the labelling was conducted in the quarantine area. Tamper proof seals were placed on the carton containers.

9. Storage and distribution

The Qualified Person was tasked for performing batch release. Each batch was tested but not necessarily released since release was performed when the batch was ready to be shipped to a specific customer. Batch certification was performed after final packaging and labelling. At the time of inspection Rifampicin was distributed abroad through brokers while for the domestic market the distribution was managed by the company's sales department.

10. Laboratory controls

A new Quality Control Center was commissioned in December 2024. The chemical laboratory was appropriately equipped, and instrumentation and glassware were adequately qualified and calibrated. The Quality Control laboratory was organized into various sections: HPLC-MS, GC, balance, IR, UV, precision instruments, physical and chemical analysis, reagent handling, sample reception, sample retention and stability rooms, and a microbiological laboratory.
Procedures for planning and conducting equipment calibration were presented.

During the visit to the analytical laboratory the following logbooks and documentation were reviewed:

- Logbook of receiving crude, recovered solvents, intermediate, raw materials.
- Logbook of disposition.
- Logbook of daily calibration, logbook of use of balance.
- SOP on Incoming material, sampling
- Test record of Rifampicin
- WHO STP for Rifampicin
- Test record of Rifamycin-S-Na
- STP of Rifamycin-S-Na
- STP of recovered Rifampicin
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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. The procedure for handling of reference/working standards was spot checked. The validity of reference standards was checked monthly and for Ph. Eur. standards a printout of the relevant web page was maintained as proof of the monthly check. Reference standards intended for assay were only used once despite the quantity remaining in the vial.
The inventory of Rifampicin Quinone CRS was checked.

OOS Handling

A procedure for handling OOS/OOT results was in place.
The logs for 2023 and 2024 were reviewed and certain OOS were selected for discussion.

Retention samples

Retention samples were maintained in Alu/LDPE envelopes, placed in carton containers, and stored in a dedicated room where temperature and relative humidity limits were established and monitored. A procedure for the retention sample management was in place and it also described the process for issuing retention samples for investigation. The retention sample logbook and daily records of temperature/humidity were spot-checked.

Stability studies

Samples were placed in a stability study and tested according to various specifications. All the specifications were covered and discussed in detail.

11. Validation

There was a qualification/validation procedure in place covering facilities, equipment, instruments, manufacturing processes, analytical methods, cleaning validation and computerized systems. The 2025 VMPs for the Site East and the Site West were briefly reviewed. In addition, the 2024 VMPs for Site West and Site East were discussed. The 2024 validation summary report for Site West was reviewed in detail. The VMP was revised annually, and the scope included qualification/validation activities to be carried out on each site.

HVAC

The HVAC system qualification report for the West Site was reviewed. Three AHUs (were supplying clean air to the Grade D area where the final steps of processing took place. AHU1-1 used 75% fresh air, AHU1-2 83%, AHU1-4 58% respectively. AHU1-1 supplied clean to the North suite where Rifampicin Polymorph I final process steps were performed. AHU1-2 and AHU1-4 were supplying air to the South suite where Polymorph II final steps were performed.
The following tests were carried out as part of the annual OQ:
Ozone generator functionality (installed in the AHU1-1)
Air changes
Temperature and Relative Humidity
Differential pressure
Leak test
Non-viable particles
Air-born Viable particles
Settle plates
The following tests were carried out as part of the annual PQ:
Temperature and Relative humidity
Non-Viable particles
Air-born viable particles
Settle plates
Moreover, the HVAC qualification report for the inoculation department and for the inoculation room grade A in East Site was discussed in detail.

Purified Water System

The PW system consisted of a potable water tank, a media column, two softeners, an activated carbon filter, a filter, heat exchanger, first pump, first RO, second pump, 2nd RO, the storage tank, the distribution loop (including 17 user points and 20 sampling points). The system was installed in November 2024. The URS was made available. The installation qualification included among other details regarding the welding of the loop. The qualification certificates of the welders were included in the report. In addition, a list of the welding points and the materials used were included in the report. Moreover, a boroscopy report was included in the IQ. Similarly, a passivation procedure and report were included as part of the IQ. NaOH 1% was used to clean the loop before passivation with citric acid 6%. Passivation of the loop was carried out for 1 hour. After passivation, the loop was washed with water until the conductivity and pH met the acceptance criteria. The PQ included three phases. Phase 1 lasted 14 days and included sampling and testing of all sampling points (20 sampling points).

Appearance, acidity/alkalinity, NO3/NO4, Chloride, SO4, NH4, oxidizable matters, heavy metals, conductivity, microbial count were the parameters monitored. Phase II lasted 14 days (07-20.12.2024) and followed the same sampling plan and parameters as Phase I. Phase III was initiated on 21.12.2024 and would last for 1 year. The sampling plan included weekly testing of 3 sampling points (outlet of the PW generation system, return loop right before the storage tank, outlet loop right after the storage tank). The remaining 17 sampling points were tested once a month.

Qualification of the autoclave

The qualification IQ/OQ/PQ of the autoclave was reviewed. The qualification included test for heat distribution (empty and with load), penetration, and leak test. The Calibration certificate of data loggers used for the qualification 4) and the procedure on Usage and maintenance of autoclave were presented.

Qualification of analytical instruments

The calibration of one of the HPLCs was reviewed. The calibration included tests for accuracy, precision, gradient performance, system precision, carry over, drift, delay volume, injector linearity, detector linearity, sample compartment temperature, column oven temperature. The validation of software Open Lab CDS was also checked. Moreover, the PQ another HPLC was presented. All HPLCs were connected to a server. Back-up was performed daily.
The IQ/OQ of two GCs were also reviewed.
The IQ/OQ/PQ of the UV spectrophotometer was also checked. The qualification included test for peak detection, spectrum evaluation, wavelength accuracy, repeatability, baseline flatness, stray light, noise level, baseline stability, baseline flatness.

12. Change control

A procedure for the management of changes was in place. The procedure was applicable to production activities, raw materials, suppliers, product specifications, computerized systems, facilities and equipment, analytical methods and any other operations that may affect the quality of the product. A list of changes for 2024 was presented. A person from the QA department was responsible for assessing the change request including input from other departments and approving/rejecting the implementation. The change control for the new QC laboratory, and the change control for the new HVAC system in the inoculation department were discussed in detail.

13. Rejection and re-use of materials

According to a written procedure reworking was not allowed.
Recovery of solvents was allowed. The only solvents that were recovered and reused in Rifampicin manufacturing process were Butanol and Acetone. Upon recovery the solvents were tested according to established specifications. Recovered solvents could present different specifications from fresh solvents provided they did not affect the process step they were used in. Approved recovered solvents could only be used for the same or previous stages from which they were recovered of the same product, according to the relevant SOP on Recovery for Butanol and Acetone.
Test records of recovered Butanol and the STP of recovered Butanol) and fresh Butanol were reviewed.

14. Complaints and recalls

There was a procedure in place for handling complaints. QA was responsible for categorizing the complaints into three classes (critical, major or minor). Annual review was performed. The complaints were recorded in a logbook. Complaints records were retained for one year following the expiry date of the relevant batch. One complaint was registered in 2022 and 2024, respectively. No complaint was registered in 2023.

The procedure for recall was presented. A recall could be categorized into first-class recall (may possibly cause severe health hazard), second-class recall (may cause temporary or reversible health hazard) and third-class recall (normally could not cause health hazard). Responsibilities and timelines for conducting investigations and taking the recall decision were established (1 day for first-class, 3 days for second-class and 7 days for third-class). The recall decision was taken by a group consisted of the Qualified Person, the Supply Manager, Production Manager, the Quality Control Manager, the Quality Assurance Manager. 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 12.2023 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 Rifampicin was not contracted out. However, the company apart from manufacturing the key starting material Rifamycin-S-Na they also purchased some quantities. The quantities originating from another supplier were assigned batch numbers that followed a different codification to differentiate from Rifamycin-S-Na batches manufactured on-site. Testing of potable water was contracted out as well as calibration of some equipment.

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, ***Hebei Xingang Pharmaceutical Co Ltd,*** *located* ***at No.2 Fuqiang Street, Zhaoyuan Road, Zhao County, Shijiazhuang, Hebei 051 530, P. R. China*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines for APIs.

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

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

Part 4	**List of GMP Guidelines referenced in the inspection report**

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

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***