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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	**Taizhou Xianju Pharmaceutical Co Ltd**
Corporate address of manufacturer	Zhejiang Xianju Pharmaceutical Co., Ltd. 15, West Fengxi Road, Modern Industrial Park, Xianju, Taizhou, Zhejiang, China, 317300
Name & address of inspected manufacturing site if different from that given above	Taizhou Xianju Pharmaceutical Co Ltd No.3 Donghai Fourth Avenue, Zhejiang, Toumen Port Economic Development Zone, Linhai, Taizhou, Zhejiang, China GPS N 28º42'11" E 121º32'59" DUNS: 421318816
Synthetic unit /Block/ Workshop	Building 9
Dates of inspection	3 – 7 July 2023
Type of inspection	Initial GMP inspection
Introduction	
Brief description of the manufacturing activities	Taizhou Xianju Pharmaceutical Co Ltd is a wholly owned Zhejiang Xianju Pharma Co., Ltd subsidiary. The former was founded in 2006 and commissioned in 2008. The site's total area is 141,800 m^2 whereas the construction area is 118,800 m^2. The main APIs manufactured on-site are Medroxyprogesterone acetate, Megestrol Acetate, Dydrogesterone, Hydrocortisone, Hydrocortisone Acetate, Methylprednisolone, Methylprednisolone Hemisuccinate, Prednisone, Ciclesonide, Budesonide, Flumetasone, Eplerenone, Vecuronium Bromide, Rocuronium Bromide, Pidotimod, Tiotropium Bromide and Sugammadex Sodium.
General information about the company and site	The parent company of Taizhou Xianju Pharmaceutical Co. Ltd is Zhejiang Xianju Pharmaceutical Co., Ltd which was founded in January 1972. The company is located at 15 West Fengxi Road, Modern Industrial Park, Xianju, Taizhou, Zhejiang, China, 317300. It has four API sites and one FDF site.
History	This was the first WHO PQ inspection of Taizhou Xianju Pharmaceutical Co Ltd. The site has been regularly inspected by the local (provincial) and central/national authorities. In addition, the site was inspected by the USFDA and MFDS.

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	The following areas were inspected: - Quality management system - Personnel and training - Buildings and facilities - Qualification and validation - Production and packaging operations - Quality control laboratories - Warehouse - Utilities
Restrictions	None
Out of scope	The scope of the inspection was limited to sterile Medroxyprogesterone Acetate (MPA) API. Other APIs and intermediates were out of the scope of this inspection.
WHO APIs covered by the inspection	APIMF419 (Sterile Medroxyprogesterone acetate)
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	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
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 (where applicable)**

1. Quality management

Taizhou Xianju Pharmaceutical Co. Ltd had a quality unit that was independent of production and fulfilled the responsibility of both quality assurance and quality control. The separate QA and QC managers reported to the site QA Director who had overall responsibility for the release of intermediates and APIs.

The Product quality review procedure was reviewed. The procedure described the scope, responsibility, and process for carrying out the product review. The review included changes, deviations, in-process controls, critical process parameters, critical quality attributes, stability monitoring, validation, OOS, OOT, reprocessing, returns, complaints, recall, contract manufacture/analysis, and follow-up of CAPA from the last PQR. The data were analyzed using a spreadsheet and the criteria of +/-3SD were set.

Management of Deviations

Deviations were managed according to the SOP for deviations. In addition, a separate SOP was used for QC-specific deviations termed “Abnormal events”. The deviation procedure was described in a flow chart and was paper-based supported by manual logbooks and tracking forms and was found to be in line with GMP requirements. The tools used for root cause analysis, the ranking of deviations

(critical, major and minor), tracking of CAPA actions and review of effectiveness were adequately described with QA performing the oversight and final approval functions.

Batch Review and Release

The responsibilities of the key QA staff for the independent review of batch manufacturing and packaging records and all associated documentation were described in SMP-PR-010. This responsibility was delegated in writing by the Qualified Person. During the evaluation of selected batch records, it was evident that the Quality Manager responsible was competent and aware of his responsibilities. The limitations of totally manual systems were evident in that over and above the batch-specific records numerous supportive reports and logbooks had to be retrieved to complete the task.

Self-Inspection

The GMP self-inspection program was adequately described by procedure which detailed the requirement that every department was inspected once per year vs ICH Q7 and the relevant ISO standards. The records for 2023 reflected that the required inspections were completed in one combined inspection by the QA department in April 2023.

Contamination control strategy (CCS)

In order to prevent the potential risk of contamination, a contamination control strategy for sterile MPA was prepared. The CCS was described under three headings such as sterility control strategy, bacterial/endotoxin control strategy and particulate control strategy. This was followed by a risk assessment and the identification of potential gaps. Additional controls in the form of revised procedures were identified.

Quality risk management (QRM)

QRM procedure was referenced to ICH Q9 and guided risk management applicable to the products manufactured by Xianju Pharma. The procedure stated the use of various tools such as FMEA, HACCP, RRF and risk priority number (RPN) was described in the procedure.

Nitrosamine impurities risk assessment

For MPA (sterile), the company performed the assessment. The risk assessment included the review of the manufacturing process including the use of various materials, solvents, reagents, potable water, and primary packaging materials. The key starting material/KSM (17-α Hydroxy Progesterone) was procured from an external supplier as well as produced on-site by Xianju. The route of synthesis for both sources was the same. The ROS confirmed that amines were used in the manufacture of KSM and that the manufacturer had performed testing on three batches of MPA and reported NDMA, NDEA and NMPA as “not detectable”.

The deficiencies noted in this section were adequately addressed and will be verified during the PQ inspections.

2. Personnel

From the opening meeting presentation, it was noted that the site employs 667 staff members for various departments in different positions. The company confirmed that they do not use the services of contracted staff. In general, good sanitization and health habits were practiced during the inspection. Staff training was performed according to the Employee Training and Assessment Procedure SMP-CM-012. In addition to the GMP requirements for API manufacture, job-specific and Health Safety and Environment (HSE) instructions, the clean room staff were also required to be trained in personal hygiene and sterile practices. There were no requirements for staff to be trained and kept up to date with relevant WHO GMP Guidelines. Departmental heads were responsible for the training on all SOP updates before implementation. Technical training was presented by specialists in each area.

The gowning and PPE provided during the synthetic processes were adequate. The gowning regime for staff working in the clean rooms for the powder processing and packaging steps was in line with the requirements for Grade C processing of terminally sterilized products. The same gowning was theoretically suitable for the processing of high-potency products where the material was contained at the source.

The deficiencies noted in this section were adequately addressed and will be verified during the PQ inspections.

3. Buildings and facilities

Taizhou Xianju Pharmaceutical Co., Ltd was separated into four sections based on their function. The administrative and living areas were situated in the south of the plant. The production area was located on the west and middle sides of the plant. QC area was located on the southwest side. The storage area was located on the northeast side. Three waste treatment areas were located on the north side. A high-level overview of the facility is as follows:

a) Building 1 (quality control)
b) Building 2 (spare one)
c) Building 3, 4, 5, 10, 13, 14, 18, 19, 20 and 21 (for synthesis)
d) Building 6 and 7 (fermentation)
e) Building 8 (admin)
f) Building 9 (for MPA)
g) Building 11 (power supply)
h) Building 12 (General Electric and maintenance)
i) Building 15 and 16 (wastewater treatment)
j) Building 17 (canteen)
k) Building 22 (warehouse)

The focus of this inspection was limited to building 9 where MPA was manufactured. In addition, other buildings were also inspected which were used for the synthesis, testing and warehousing. Building 9 was dedicated to the manufacturing of three Progestogen API's i.e. Sterile.

Medroxyprogesterone acetate (MPA) and Megestrol Acetate which shared common manufacturing equipment and Dihydrogesterone which was manufactured on dedicated equipment. In general, the

buildings and facilities used for the manufacture of MPA were located, designed, and constructed to facilitate cleaning and maintenance with adequate space. The laboratory and production areas were in different buildings.

The “clean room area” of Building 9 was designed for the manufacture of sterile MPA in a Grade C/A environment for bioburden control and the containment of MPA as a hazardous substance. The change room design and positioning of processing rooms and supporting areas were generally in compliance with the requirements.

The deficiencies noted in this section were adequately addressed and will be verified during the PQ inspections.

4. Process equipment

From the visit to the synthesis and powder processing areas, it was noted that the equipment used in the manufacture of intermediates and APIs were of appropriate design and adequate size, and were suitably located for their intended use, cleaning, sanitization, and maintenance. Various reactors (SSR, GLR and Hastelloy) were used according to the types of reactions which were considered adequate. The lines used for the transfer of materials and solvents were adequately identified with names and direction signs. Logbooks were maintained for the usage of reactors, crystallizers, and other equipment.

The calibration of control, weighing and measuring devices was performed in-house by the engineering team. The calibration tags confirmed the last calibration and next calibration due dates. The equipment used for production and packaging areas were equipped with HMIs. These HMIs were used for the operation and transfer of in-process materials in closed conditions from one stage to another stage.

The deficiencies noted in this section were adequately addressed and will be verified during the PQ inspections.

5. Documentation and records

A manual system of documents was in place. All documents reviewed during the inspection bore a unique document number, version number and effective date and all were adequately signed/dated and approved.

The deficiencies noted in this section were adequately addressed and will be verified during the PQ inspections.

6. Materials management

Written procedures for the chronology of material management were available. There was a system in place to evaluate suppliers of materials and confirmation of the approved supplier was performed on receipt. The total area of the warehouse was 9600m^2 which was divided into an API warehouse, packaging materials warehouse, solid warehouse, liquid warehouse, reagent warehouse, solvent tank area, hardware warehouse and engineering warehouse. Incoming solid starting materials, finished APIs and Intermediates, excipients and packaging materials were stored in dedicated areas. Control of the quality status of materials (quarantine, approved and rejected) was achieved by a combination of dedicated storage areas per category and status labels, supported by manual stock cards and paper-based transactions. The temperature distribution of the various warehouses had been mapped, with 4 worst-case monitoring points identified per area.

The deficiencies noted in this section were adequately addressed and will be verified during the PQ inspections.

7. Production and in-process controls

Inspectors visited building number 9 and inspected the material transfer and synthesis areas. Trolleys were used to transfer solid materials from the warehouse building to the MPA building. The large-volume solvents were transferred through fixed pipelines connected with the tank farm whereas small-volume solvents were transferred in drums to the MPA building. The materials were charged through gravity from the 4th floor, with the 3rd floor used for synthesis and powder processing, the 2nd floor for centrifugation and drying and the 1st floor as an auxiliary area. A glovebox was provided for the charging of pyridine. MSDS were available for the mentioned solvents. Upon a visit to the temporary intermediate storage area, it was noted that several batches of intermediate 2 were stored with a retest period of 2 years. Similarly, a hold time of 15 days was assigned to intermediate 1. On the 3rd floor, crude MPA was transferred in closed condition to the GLR. The temperature sensor and RPM calibration were performed in-house, and the lines were colored with directional signage. Inspectors visited building number 9 and inspected the powder processing area used for MPA. The incoming line was fitted with a 0.22µm filter which was changed every production campaign (not more than 10 batches). At the time of the inspection, there was no production activity being carried out.

The deficiencies noted in this section were adequately addressed and will be verified during the PQ inspections.

8. Packaging and identification labelling of APIs and intermediates

Packaging integrity testing of the 3-bag system was confirmed by microbiological ingress studies in May 2023. These studies confirmed the critical process variables of the in-line sealer which were set via the HMI, however, there was no documented confirmation of the seal integrity of the second and third PPE bags during filling. There was also no in-process sampling and testing of the fill mass during the packing process. After exiting the isolator, the sealed bags were passed through a “pass box” into the secondary packaging area where they were labelled and packed into fibre drums before being transferred to the warehouse under quarantine. After QA release, the bags of material were sent back to the secondary packaging area where the labels were removed from the bags before being placed into aluminium containers to which the final product label was attached. Two tins were then placed into a cardboard box before being sent for sterilization by gamma irradiation at an outside contractor. The irradiated boxes were returned to the Company with irradiation indicator labels. The

certificate of irradiation was reviewed by QA versus the specification before the sterile MPA product was released for supply. The records of this process together with line clearance documentation were found to be adequate.

The deficiencies noted in this section were adequately addressed and will be verified during the PQ inspections.

9. Storage and distribution

Finished goods were distributed from the integrated warehouse described in Section 6 above.

10. Laboratory controls

The QC department was responsible for the testing of raw materials, packaging materials, in-process control, testing of intermediates and final products, management of reference standards, stability tests, retaining samples etc. Analytical instruments for different types of testing such as IR, UV, GC and HPLC were available in the QC department. A centralized quality control laboratory was housed in building number 1 which served all production activities. The QC laboratory was staffed with 39 members including 5 microbiologists. In addition, 5 QA staff provided support for the review of data.

Out of Specification and Out of Trend Management (OOS)
OOS were managed according to the OOS/OOT Investigation Procedure which referred to relevant US FDA and MHRA Guidelines. There was a clear flow chart for Chemical testing OOS which reflected a standard three-phase approach to investigations supported by clear statistical ranges for the interpretation of retest results. There was an equivalent SOP for microbiological testing OOS which followed a similar but adapted approach. Following a review of the procedure and selected examples it was observed that although the SOP was well described and rigorous the decision to resample was made before the possibility of an analytical error had been robustly investigated and discounted.

Microbiology laboratory located at FDF site
An inspector visited the FDF facility of Zhejiang Xianju Pharma to assess sterility testing performed on sterile MPA. The microbiology laboratory was located on the 5th floor. The entire floor was dedicated to microbiology testing activities. A total of three sterility areas were available, one each for direct inoculation method, membrane filtration method and MPA testing. Separate airlocks were provided for material and personnel wherein sterility testing was performed under LAF (Grade A) with a Grade B background. The environmental monitoring was performed simultaneously whereas finger dabs were collected for personnel monitoring from the microbiologist. The sterile MPA was tested using the direct inoculation method. It was informed by the company that there had not been any sterility failure for more than 10 years. Separate rooms were available for media preparation, autoclave, positive controls, microbial limit test and bacterial endotoxin test. The microorganisms were handled under a biosafety cabinet. The LAF was requalified once every 6 months.

The deficiencies noted in this section were adequately addressed and will be verified during the PQ inspections.

11. Validation

Validation master plan 2023 Taizhou Xianju was discussed. It stated that risk assessments were required for the building, facility, equipment, and utility system before requalification was performed. It was noted that the manufacturing process was revalidated every 5 years.

Cleaning validation

The cleaning validation procedure referred to the use of LD50, 10ppm and maximum daily dose in addition to the PDE approach. From the list of products requested, it was noted that the site manufactured 22 APIs of different therapeutic areas.

Process validation

Detailed procedure for the implementation of process validation was discussed. The procedure guided the contents to be included in the PV protocol before proceeding with the PV. The procedure stated that PV should be implemented prospectively and concurrently taking at least three consecutive batches. The procedure described criteria of +/-3SD. In 2023, the company revalidated the manufacturing process of MPA (non-micronized to sterile MPA) due to the introduction of a new multimill. The validation protocol was reviewed. Three batches were taken to validate the process and equipment listed in the report. The samples were taken from the start, middle and end of the multimill operation and the samples were tested for particle size and assay. All results reported were well within the limit. Similarly, after the micronisation, samples were taken for particle size distribution and assay and were reported to be within the limit. For gamma radiation, samples of three batches were sent to the outsourced provider and results were reported within the limit.

Gamma radiation sterilization

The sterilization validation (gamma radiation) for micronized MPA was performed between Sept and Nov 2019 and three validation batches were taken. The gamma radiation was outsourced, and critical process parameters were identified. The radiation dosing range for three batches was verified. The test results before/after sterilization were tabulated and reported to be within the limit (sterility after sterilization and other parameters). In addition, the dosing range for three batches was tabulated and it was noted that the gamma radiation dose confirmed a SAL of $10^{-}6$ (ISO 11137-2:2013 stated that the sterilization dose for MPA. Performance qualification (dose mapping) of MPA by gamma sterilization was outsourced in October 2019. The company reported that process validation for the process steps starting with the addition of key starting material through to the manufacture of non-micronized MPA was carried out in 2022.

Computer system validation

The procedure for computerized system management in the production area was discussed.

Analytical method validation

The company confirmed that analytical methods for all tests used in MPA analysis had been validated. For example, related substances, impurity F, PSD, residual solvents, bacterial endotoxins, sterility test (at FDF site), residual Benzene and Carbon tetrachloride. The test methods had been validated on-site by the Quality Research Group located within the quality control laboratory. The analytical method validation (AMV) report for related substances test of MPA was discussed. The AMV report listed the validation activities as system suitability, precision, specificity, LOQ, LOD, linearity, accuracy, intermediate precision, repeatability, solution stability and method robustness.

The robustness included the change of flow rate, column temperature, HPLC column, wavelength, and mobile phase ratio. The report concluded that small changes in wavelength, flow rate or mobile phase ratio had no adverse impact on the result of the related substance test. In addition, intermediate precision was performed by injecting the same solution into two different HPLC systems (Agilent and Shimadzu) with the results within acceptable limits.

The deficiencies noted in this section were adequately addressed and will be verified during the PQ inspections.

12. Change control

Change control was managed by the SOP which defined the requirements across the entire company. The system was managed by QA with paper-based standard formats and handwritten entries with a total of 99 change controls opened since January 2022 of which 7 related to MPA. There was a clear set of criteria for the categorization of change controls into Critical, Major or Minor. The Head of Department of the area concerned identified the impacted departments which was then verified by QA before circulation. An FMEA risk-based tool was used to assess the impact of the proposed change and the assignment of actions. The QA representative monitored the completion of to plan and the effectiveness of change and summarized the data on an annual basis into the various categories of change and the number of change controls per department. Target completion times were determined per event and were monitored by QA.

The deficiencies noted in this section were adequately addressed and will be verified during the PQ inspections.

13. Rejection and re-use of materials

The master production instructions for various stages provided details about the recovery of solvents and their use back in the manufacturing process as follows:

- Stage 5 recovered DMF (to be used in Stage 3);
- Stage 6 and 7 recovered DCM and Methanol (to be used in Stage 7).
- All solvents were recovered on-site and not outsourced.

The company confirmed that they have not performed any blending activity as the current batch size meets the customer’s requirement. Also, the company confirmed that reworking was not allowed and that no reworking had been performed.

The deficiencies noted in this section were adequately addressed and will be verified during the PQ inspections.

14. Complaints and recalls

Complaints and recalls were managed according to the procedure. The procedure was supported by a detailed flow chart which outlined the various steps. The targets for the initial confirmation, investigation and completion of corrective actions were 3,15 and 30 working days respectively, which resulted in a maximum customer response time of 48 working days. There was a clear

requirement for the consideration of other related batches when quality issues were confirmed and for all customers and relevant Regulatory Authorities to be contacted. A total of 12 justified complaints were received in 2022 with 2 received in 2023 all of which have been closed with no suspension of sale or recall required. There were two complaints received for sterile MPA none of which were of concern. The complaints procedure was supported by the returned product handling procedure.

The procedure for product recalls described the process which was managed by the Quality Director with a target for local and international recall completion of 30 and 60 days respectively. No recalls had been instituted with the most recent mock recall completed in December 2020 which was within the three years stipulated in the SOP.

The deficiencies noted in this section were adequately addressed and will be verified during the PQ inspections.

15. Contract manufacturers (including laboratories)

Contract Manufacturing was managed following the procedure which included clear steps for the initial assessment of the supplier's capability to perform the work followed by a formal assessment process via a combination of desktop and physical audits. The requirements for technical agreements and sharing of technical information were also described. The assessment process, the Quality agreement, the irradiation sterilization agreement, the irradiation and sterilization management procedure and the most recent on-site audit report from April 2023 were evaluated for the Gamma irradiation facility and found to be in order.

Contract testing was managed per SOP which applied to all forms of outsourced testing. The contract testing agreement, the relevant specification and the most recent on-site audit report from May 2023 for the outsourced sterility testing of MPA to Zhejiang Xianju Co Ltd Drug Product Department were found to be in order.

Suppliers of starting materials were managed per SOP which described the process from initial evaluation to final approval of the supplier through to ongoing monitoring of performance. The records and contract for the supplier of 17 alpha hydroxy Progesterone (code T004) as well as the Supplier Annual Assessment from October 2022 were reviewed and found to be in order. The assessment confirmed that one batch of intermediate was rejected in 2022 following an OOS investigation.

The deficiencies noted in this section were adequately addressed and will be verified during the PQ inspections.

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, ***Taizhou Xianju Pharmaceutical Co Ltd*** located ***No.3 Donghai Fourth Avenue, Zhejiang, Toumen Port Economic***

Development Zone, Linhai, Taizhou, Zhejiang, 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 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://www.who.int/publications/m/item/trs986-annex2

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
   https://www.who.int/publications/m/item/annex-2-trs-957

3. WHO guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report. Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 9.
   Short name: WHO TRS 1010, Annex 9
   https://www.who.int/publications/m/item/trs1010-annex9

4. 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
   https://www.who.int/publications/m/item/annex-3-trs-1033

5. 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://www.who.int/publications/m/item/annex-4-trs-929

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. 957, Annex 1
https://www.who.int/publications/m/item/trs957-annex1

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://www.who.int/publications/m/item/trs957-annex3

8. 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://www.who.int/publications/m/item/Annex-8-trs-1010

9. 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
https://www.who.int/publications/m/item/trs1019-annex2

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
Short name: WHO TRS No. 1044, Annex 4
https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/production/trs1044-annex4-technology-transfer-in-pharmaceutical-manufacturing.pdf

11. WHO good manufacturing practices for sterile pharmaceutical products. Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
Short name: WHO TRS No. 1044, Annex 2
https://www.who.int/publications/m/item/trs1044-annex2

12. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-First Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. ***Short name: WHO TRS No. 943, Annex 3***
https://www.who.int/publications/m/item/trs943-annex3

13. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2.
Short name: WHO TRS No. 961, Annex 2

https://www.who.int/publications/m/item/trs961-annex2

14. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2.
Short name: WHO TRS No. 981, Annex 2
https://www.who.int/publications/m/item/trs981-annex2

15. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3.
Short name: WHO TRS No. 981, Annex 3
https://www.who.int/publications/m/item/annex-3-trs-981

16. WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14.
Short name: WHO TRS No. 961, Annex 14
https://www.who.int/publications/m/item/tr961-annex14

17. Good Manufacturing Practices: Guidelines on validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3.
Short name: WHO TRS No. 1019, Annex 3
https://www.who.int/publications/m/item/trs1019-annex3

18. WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4.
Short name: WHO TRS No. 992, Annex 4
https://www.who.int/publications/m/item/trs992-annex4

19. 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://www.who.int/publications/m/item/trs961-annex9-modelguidanceforstoragetransport

20. 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.
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