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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	**Chongqing Carelife Pharmaceutical Co. Ltd.**
Corporate address of manufacturer	Chongqing Carelife Pharmaceutical Co. Ltd. Site II No.2, The Third Branch Road, Huanan Road, Yan Jia, Changshou District, Chongqing 401221, P. R. China
Inspected site	
Name & address of inspected manufacturing site if different from that given above	N/A
Synthetic unit /Block/ Workshop	Workshop 102
Inspection details	
Dates of inspection	11-14 December 2023
Type of inspection	Initial inspection
Introduction	
Brief description of the manufacturing activities	Chongqing Carelife Pharmaceutical Co. Ltd. Site II manufactures and distributes active pharmaceutical ingredients for the Chinese market and foreign markets, including USA, Europe, India, Brazil, Indonesia, Japan, and Egypt. The site consists of 6 buildings: Building D includes Workshops 101, 102, 103 and 104. Buildings B, C, and E are warehouses for different materials. Building A includes the QC laboratories and office areas, while the waste-water treatment plant is located in area F. At the time of inspection several new workshops were under construction.
General information about the company and site	Chongqing Carelife (thereafter Chongqing Carelife) was established in July 2000. It is an export-oriented company and a subsidiary of Yaopharma since 2009, specializing in the manufacture of APIs. The company has two sites. Chongqing Carelife Site II is located at the Chongqing Changshou chemical & industrial zone, approximately 80km

	from Chongqing, and 70km from the airport. This site is responsible for the manufacture of Nirmatrelvir API (Workshop 102).
History	This was the first WHO prequalification inspection. The site is periodically inspected by the Chongqing Drug Administration. The site was also inspected in July 2019 by USFDA
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Pharmaceutical Quality System Documentation Facilities and Equipment (warehouses, workshops) Utilities Production Packaging and labelling Product Release Quality Control laboratories
Restrictions	N/A
Out of scope	APIs not submitted for Prequalification were excluded from the scope of this inspection
WHO APIs covered by the inspection	Nirmatrelvir
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**

1. Quality management

The company had established a QMS based on WHO GMP guidelines, USFDA regulations, NMPA regulations and ICH guidelines. The principles of the system were described in the Quality Manual. In general, personnel had the necessary experience and were appropriately trained. Facilities and equipment were adequately maintained and qualified. A documentation system was in place. Quality risk management was integrated in all aspects of the QMS, and the basic concepts were aligned with ICH Q9. Senior management responsibilities and commitment were defined.

Quality Risk Management

The principles of QRM were described in high level in the QM and indicated that they were applied to all GMP related operations and activities. A written procedure was in place. The following risk assessments were reviewed in detail:

- Potential formation of Nitrosamines during manufacturing of Nirmatrelvir. This was the second version which was generated upon transfer of the product from R&D to production. The first version was generated by R&D and was submitted as part of the dossier.
- Nirmatrelvir production in a multiproduct facility (Workshop 102)
- Palbociclib production in multiproduct facility (Workshop 102)

Product Quality Review (PQR)

The SOP for PQR was made available. The 2022 Nirmatrelvir PQR was reviewed. Nirmatrelvir was introduced in Workshop 102, in April 2022 (submission to WHO in July 22). The batch size was 40 kg. In total, 4 batches were manufactured, the first one was an exhibition batch manufactured for scale up purposes and process improvement. Three more batches were manufactured for process validation. The total quantity manufactured was 153.070 kg.

Batch release

The company had established a procedure for batch release. The procedure defined the process for release of intermediates, finished products and R&D finished products.

The release of intermediates intended for in-house use, was delegated to Production. More specifically the QC had to review the analytical work including deviations and OOS using a checklist. Then the QC forwarded the CoA to the relevant Workshop which was responsible for reviewing the BMR data and the CoA and verifying that OOS and deviations had been closed out. Finally, the Workshop would release the intermediate for further processing.

The process of release for intermediates intended for sale and APIs, involved a review of the BMR and any deviations during manufacturing performed by Production and verified by the QA. A review of the analytical records including OOS, deviations, and any abnormal test results was performed by the QC and verified by the QA. The release template included a confirmation by the QA that all changes, deviations, and OOS had been adequately addressed and a final release signature by the QP.

In relation to Nirmatrelvir API release, and according to Chongqing Carelife, the site was responsible for performing finished product testing. The CoA along with any non-conformance investigation during production or testing, if any, would be sent to Fosun. Fosun would certify or reject the batch and communicate its decision to Chongqing Carelife for releasing the batch.

Deviations

A procedure for handling deviations was in place and was discussed in detail. The SOP defined a deviation as any excursion from approved instructions or established specifications. Operators identifying a deviation had to report it as soon as possible to their supervisor and the QA department. A template was used to report deviations and was available at department level (issued by the department supervisor). Upon reporting, the department head could apply immediate remedial measures and transfer the deviation to the QA department within 24 hours. The QA department was responsible for checking for recurrence, conducting an initial impact assessment, and classifying the deviation. A root cause investigation would be initiated, and the QA would convene a team to perform a risk assessment. Considering the outcome of the risk assessment the classification of the deviation

could be revisited. Actions related to material or product had to be established including a detailed CAPA plan. The effectiveness of CAPA had to be evaluated after implementation. Examples of registered deviations were reviewed.

All the non-compliances in relation to Quality Management were addressed by the manufacturer, to a satisfactory level.

2. Personnel

There were approximately 400 employees working on site. Production operated in two 12-hour shifts. Key personnel responsibilities were described in job descriptions and the hierarchical and administrative structure were depicted in organization charts. Induction and continuous training were provided in accordance with the procedures for employee training, and training plans, and evaluation records were maintained. Training sessions were delivered by appropriately qualified trainers. The SOP for training was made available. There were 3 types of training, focusing on new employees, existing employees (including employees changing position), and training after a long leave (more than 90 days). An example of a new employee training record was reviewed.
Additionally, the following job descriptions were presented:

- Manager of Quality Assurance Department. She joined the company in 2013 and became QA Manager in 2021.
- Qualified person. He joined the company in 2004 and became QP in 2019.
- Manager of workshop. He joined the company in 2007 and became the Manager in 2017.
- Operator in workshop 102

Personnel Hygiene

The SOP for Management of occupational health surveillance system was presented. Personnel involved in GMP activities had to periodically undergo health examinations according to the Chinese regulations.

All the non-compliances in relation to Personnel were addressed by the manufacturer, to a satisfactory level.

3. Buildings and facilities

The campus consisted of several buildings and workshops. Layouts of the facilities were made available. In general, premises were constructed, designed, and maintained to suit the operations to be carried out and prevent the risk of contamination of materials and products. At large, the design of premises was such as to minimize the risk of errors and permit effective cleaning and maintenance. The table below provides the list of buildings:

Code	Building – Activity
A	Administrative building -3rd floor QC laboratories
B	Annex of the administrative building finished product warehouse I
C	Power supply – Solid raw material warehouse II
D	Workshops 101, 102, 103, 104
E	Solvents and liquids warehouse III
F	Wastewater treatment

Nirmatrelvir API was manufactured in Workshop 102 which consisted of 3 floors and was not product dedicated. The top floor was assigned to the synthesis and production of APIs and that was where most

of the reactors and addition vessels were installed. The second floor was dedicated to processing steps, including filtration, centrifugation and drying. The clean area (Grade D) where the final processing and purification steps took place was located on the first floor (ground floor). Access to the top two floors of workshops 101 and 102 was through the same staircase but different entries on each floor. Access to the clean area of workshop 102 was dedicated.
Dispensing of materials took place on the third floor of workshop 102.
As indicated on the table above, the company had dedicated warehouses for solid raw materials, liquids and solvents, and finished products. Temperature was monitored and controlled (<30°C) in the raw material warehouses while relative humidity was not controlled. For temperature sensitive finished products, a cold room was available (2-8°C).
At the time of inspection several new buildings were under construction.

All the non-compliances in relation to Facilities were addressed by the manufacturer, to a satisfactory level.

4. Process equipment

Reactor systems, equipment, and utilities were installed to allow reflux, distillation, cooling, crystallization, centrifugation, drying, and milling required to make the APIs of interest. Materials of product contact were suitable. Tools and equipment were uniquely identified, and status labels were generally used. Similarly measuring equipment were labelled including calibration status. In general, they were maintained according to written procedures and a plan for preventive maintenance was available. For processing equipment, a detailed annual preventive maintenance was in place while a monthly check on the motor was also performed. Both maintenance activities were adequately documented. Spot checks on the preventive maintenance of glass reactors, centrifuges and addition vessels were made. Dedicated flexible hoses and centrifuge bags were used for each intermediate and production stage. They were appropriately stored in metal cabinets on the third floor and labelled.

The SOP for cleaning of the equipment used for Nirmatrelvir in the clean area was made available. The cleaning process described in the procedure was not aligned with the process that was followed. The reactor on the second floor was directly connected to the crystallization reactor in clean area (first/ground floor) which was further connected to the centrifuge. There were no other pipes to discard waste solvents. Thus, by design, waste solvents from less clean process steps/equipment (reactor on second floor) were introduced to equipment used for final purification processes (crystallization, centrifugation). The risk of contamination had not been assessed.

All the non-compliances in relation to Equipment were addressed by the manufacturer, to a satisfactory level.

5. Documentation and records

The company used a hard copy documentation system. There were procedures in place for issuance, approval, control, review, and withdrawal of procedures and quality documents. Procedures had to be reviewed every two years, unless otherwise required. Material and product specifications were detailed in written form. Similarly, analytical methods for each material and product were documented.

Batch numbering system

There was a procedure in place for issuing batch numbers. The Workshop Supervisor was responsible for generating the batch number during the work order. The Workshop Head and the QA department were responsible for verifying and approving the batch number. There were different rules for generating batch numbers for intermediates and finished products, reworked, reprocessed, validation and recovered solvent batches. The codification for finished products consisted of 4 parts. The 1st part reflected the product code and was only letters, the 2nd part reflected the year (4 digits), the 3rd part the month (2 digits), and the last part consisted of consecutive numbers representing the bath number per month (3 digits/month).

All the non-compliances in relation to Documentation were addressed by the manufacturer, to a satisfactory level.

6. Materials management

There was a material management procedure in place. A checklist was used for the receipt of raw materials. Three warehouses (warehouse I, warehouse II, warehouse III) were established. In warehouse I, packaging material, labels, finished products and intermediates for sale were stored. In warehouse II, solid raw materials and intermediates for in-house use were placed. Warehouse III was used for liquid raw materials (4 rooms, 1st room general solvents, 2nd room section 1: alkaline liquids and section 2: general solvents, 3rd room section 1: general solvents – controlled under Chinese legislation, section 2: general solvents, 4th room: section1: acids, section2: acids)
The Environment, Health, and Safety Department (EHS) was responsible for establishing the list of materials according to their characteristics (acid, base, toxic, flammable, etc.) which was used by warehouse personnel to place each material in the assigned warehouse. The responsibility and detailed instructions on the use of MSDS to establish the list, were described in a written procedure.
A dispensary for solid raw materials was established on the third floor of workshop 102. Dispensing took place in accordance with a written procedure. Dispensing of liquid materials took place on the production floor and was performed by weight.

All the non-compliances in relation to Materials Management were addressed by the manufacturer, to a satisfactory level.

7. Production and in-process controls

The production operated in two 12-hour shifts. In general, production operations followed defined procedures. Process flows and routes of synthesis were available. Access to production premises was restricted to authorized personnel. Entry to the third floor of workshop 102 was done through a change room. Calibration procedures and records for scales were presented. Closed systems and dedicated pipes were used for material transfers from reactors to centrifuges. Examination of the flow of the manufacturing process and relevant equipment was in line with the BMRs checked during the inspection. There were procedures in place for cleaning and sanitization of premises and equipment and records were maintained.

The inspector visited workshop 102 and observed the dispensing and charging activities on 12.12.2023 and the crystallization, centrifugation and washing activities on 14.12.2023. Additionally, the clean area on the ground floor was visited.

The procedure for blending API batches was reviewed and discussed in detail. Blending of batches manufactured within a 6-month period was allowed. The expiry date of the blended batch was assigned based on the eldest batch. Full testing of the batch was performed before release. A stability study had to be carried out for the first blended product batch. Tail batches used for blending were labelled and stored in the same way as finished products.

All the non-compliances in relation to Production activities were addressed by the manufacturer, to a satisfactory level.

8. Packaging and identification labelling of APIs and intermediates

The procedure for Nirmatrelvir packaging was discussed. Nirmatrelvir API was packed in double PE bags under a booth in the clean area on the ground floor of Workshop 102. Then the API was transferred to the secondary packaging area where the double bags were placed in an aluminium foil bag and then in a carton drum. Several labels were used during primary and secondary packaging, but the information and their use and function were not adequately defined in the procedure. Additionally, a tamper-evident seal was used to secure the paper drum and its number was recorded in the BPR according to a written procedure.

All the non-compliances in relation to Packaging activities were addressed by the manufacturer, to a satisfactory level.

9. Storage and distribution

A warehouse for the storage of finished products and intermediates for sale was established (warehouse I). The warehouse consisted of several rooms used for the storage of primary packaging material (<30°C), secondary packaging material (<30°C), finished products stored at 15-25°C, finished products stored at 0-30°C, returned, and recalled products. There was also a cold room (2-8°C) and a freezer (<0°C).

All the non-compliances in relation to storage and distribution activities were addressed by the manufacturer, to a satisfactory level.

10. Laboratory controls

The quality control laboratories were located on the third floor of the administrative building. Samples were received at the laboratory according to an established procedure. The sample was checked, verified, and registered in a logbook. The quantity of the sample to be withdrawn during sampling was defined in the material test procedure. Reconciliation of sample quantity took place after testing for solid raw materials but not for liquids/solvents. Analytical methods and records related to Nirmatrelvir were reviewed in detail.

Retention samples were stored in a dedicated room where temperature and relative humidity were controlled and monitored (T: 15-30°C, RH<75%). A procedure for maintaining and handling retention samples was in place. According to the procedure retention samples for poisonous, toxic, volatile, and explosive starting materials were not maintained. The storage period was defined according to the material category. For finished products retention samples were maintained for 3 years after expiry.

There were two dedicated rooms where 9 and 5 stability chambers were installed respectively. All stability conditions were covered, including cold room conditions (2-8°C). Printouts of stability conditions for each chamber were maintained in a logbook. In case of malfunction an alarm would be triggered, and 3 persons would be notified by SMS. The alarm system was challenged annually. The latest report was reviewed.
A procedure was in place for defining stability studies activities. A plan for stability testing for all APIs/intermediates in stability studies would be compiled monthly and the date of sample withdrawal would be recorded in a logbook. According to the procedure, samples in long-term stability studies could be withdrawn up to 7 days after the due date while samples in accelerated stability studies could be withdrawn up to 3 days after the due date.
The stability of Nirmatrelvir Intermediate 2 (NT2) was reviewed. Three batches were placed in stability. Appearance, specific impurity, individual unspecified impurity, total impurities, and assay were identified as stability indicating parameters. Testing was performed at release, 1, 3 and 6 months. Results for all time points were found within specifications.

All the non-compliances in relation to Laboratory activities were addressed by the manufacturer, to a satisfactory level

11. Validation
There were procedures in place and a Validation Master Plan describing the basic concepts of validation. The procedure was applicable to qualification/validation activities including but not limited to buildings, facilities, equipment, production processes, cleaning, disinfection, and computerized systems.

Cleaning validation
The validation report of equipment cleaning for Nirmatrelvir was reviewed. As part of the cleaning validation, clean hold time studies were carried out for all major equipment including flexible hoses and utensils used in the production of Nirmatrelvir in workshop 102. Particulate contamination was evaluated by visual inspection at 1, 5, 7, 9 days. The approach for visual inspection of particulate contamination was not fully justified. Microbial clean hold time study for equipment found in the clean area (Grade D) was carried out for 3 days. Supportive data was presented. Dirty hold time study for 12 hours was also carried out. Following the study instructions were established to clean equipment within 12 hours of use.

Process validation
The validation report for the manufacturing process of Nirmatrelvir was reviewed. This was the 2nd version of the report. The 1st version of the report was submitted to WHO. The updated report was compiled due to an update in IPC and FPP specifications, but it had not been submitted to WHO. Three batches were manufactured and evaluated. Additionally, a demo batch was manufactured but the data had not been included in the original or the updated report.

Centrifuge requalification

The Operation Requalification Report for a Centrifuge was reviewed. Qualification documentation, empty run, calibration of standard equipment, sealing, rotational speed, safety, and protection were included as part of the OQ requalification. The calibration certificate of the standard tachometer was presented.

All the non-compliances in relation to Qualification/ Validation activities were addressed by the manufacturer, to a satisfactory level

12. Change control

A procedure for change management was presented. The SOP was applicable to all GMP related activities including but not limited to, site/facilities, process, batch size, specifications, test method, storage, expiry date, packaging, material supplier, computerized system, production and laboratory equipment devices, utensils, utilities, cleaning methods, outsourced services, authorized person, documentation.

Department supervisors were responsible for initiating a change request and record it on a template issued by the QA department. The department head was responsible for signing the request. The request would then be sent to the QA department for circulation to the affected departments for their evaluation. Then the QA convened a team to conduct a risk assessment. Considering the results of the risk assessment the QA department would categorize the change request according to the impact as major, moderate, or minor. At this stage the request could be approved or rejected. A plan for the implementation would be established, including deadlines. The QA department was responsible for verifying the implementation and the effectiveness of the change.

All the non-compliances in relation to Change Control were addressed by the manufacturer, to a satisfactory level

13. Rejection and re-use of materials

Recovery of solvents for Nirmatrelvir did not take place.

The procedure for reprocessing or reworking was reviewed. Reprocessing could only take place if the water content, particle size and residual solvents did not meet the specifications. No risk assessment was necessary since the process steps to be carried out were part of the manufacturing process and did not include any reaction steps. A long term stability study was considered only for the first batch presenting an OOS result in water content, particle size and/or residual solvents.

Reworking was handled on a case-by-case basis. A risk assessment had to be carried out. The impurity profile of the reworked batch was compared to a normal batch and the reworked batch was placed in a long-term stability study.

The Head of the Quality Centre was responsible for taking the decision on reprocessing or reworking of a batch.

The procedure for handling rejected materials/products was presented. A definition of rejected material/product was included in the SOP. The procedure defined that raw materials that did not meet the specifications upon receipt could be rejected and returned to the manufacturer/supplier, while raw materials stored at the warehouse but not meeting the specifications after re-testing were discarded. For intermediates and finished products not meeting the specifications there were three possibilities: reprocess, rework or disposal. A procedure for disposal was available. Materials and products for destruction were isolated and stored in a dedicated area. The Environment, Health and Safety Department was responsible for the disposal according to a written protocol.

All the non-compliances in relation to rejection and reuse of materials were addressed by the manufacturer, to a satisfactory level.

14. Complaints and recalls

Complaints could be received by different people in several departments. According to the procedure the recipient of the complaint had to communicate the complaint information by Email to the QA department which was responsible for registering the complaint. After confirmation of the complaint, a root cause investigation would be initiated, recurrence would be checked, and investigations would be extended to different batches and/or products depending on the nature of the complaint and root cause. CAPA would be identified and applied including the initiation of the recall process. The effectiveness of CAPA would be evaluated.

The decision for recall was taken by the QP. The recall was categorized in 3 classes (I, II, or III) depending on impact on patient health and urgency. The recall team was convened to manage the different activities related to the recall and reported to the QP. Timelines for completing the recall were defined in each recall protocol considering different parameters including but not limited to the number of batches, distribution, etc. The effectiveness of the recall had to be evaluated upon completion.

A mock recall was carried out every 3 years. Criteria for the selection of the API to be used in the mock recall were defined. The last mock recall was carried out in 2021.

All the non-compliances in relation to complaints and recalls were addressed by the manufacturer, to a satisfactory level.

15. Contract manufacturers (including laboratories)

No manufacturing step of Nirmatrelvir was contracted out.

All the non-compliances in relation to technical agreements were addressed by the manufacturer, to a satisfactory level.

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, ***Chongqing Carelife Pharmaceutical Co. Ltd. Site II.***,located at ***No.2, The Third Branch Road, Huanan Road, Yan Jia, Changshou District, Chongqing 401221, 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 WHO 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-eighth 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. Fifty-seventh Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052), Annex 4.
Short name: WHO TRS No. 1052, Annex 4
https://www.who.int/publications/i/item/9789240091030

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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