World Health Organization

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

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

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**ST Pharm Co. Ltd.**
Corporate address of manufacturer	7 F i-Park Tower, 520, Yeongdong-daero, Gangnam-gu, Seoul 06170 Republic of Korea
Inspected site	
Name & address of inspected manufacturing site if different from that given above	**ST Pharm Co. Ltd. (Sihwa)** 231 Hyeomnyeok-ro, Siheung-si, Gyeonggi-do, 15086 Republic of Korea GPS Coordinates 372054.2N 1264244.6E
Synthetic unit /Block/ Workshop	Plant 5
Inspection details	
Dates of inspection	14-15, 18 September 2023
Type of inspection	Routine GMP inspection
Introduction	
Brief description of the manufacturing activities	ST. Pharma is a contract manufacturer of small molecules, especially APIs and their intermediates, as well as oligonucleotides. ST Pharm does not manufacture any toxic or hazardous materials. The site's manufacturing portfolio includes among others antihypertensives, antivirals, antibiotics, and statins.
General information about the company and site	Samchully Pharmaceutical Co. Ltd was established in 1983 and started producing bulk pharmaceutical chemicals in 1987. In June 2010 it became a subsidiary of Dong-A Socio Group and in October 2010 changed its name to ST Pharm Co. Ltd. The ST Pharm Co. Ltd. Sihwa site is located approximately 40Km south-west of the Incheon International Airport. The site was licensed by MFDS to manufacture APIs and their intermediates in 1998.
History	This was the first WHO inspection. A desk assessment was carried out in September 2019. The site had been inspected in the past by USFDA and PMDA. The site is regularly inspected by MFDS.
Brief report of inspection activities undertaken – Scope and limitations	

Areas inspected	Pharmaceutical Quality System Documentation Facilities and Equipment (warehouses, tank farm, plant 5, laboratories) Purified Water System Production Quality Control Packaging and labelling Product Release
Restrictions	N/A
Out of scope	Products not submitted for WHO prequalification. The company informed the inspectors of the discontinuation of Sofosbuvir API and Terizidone API production. Therefore, these APIs were not covered by this inspection.
WHO APIs covered by the inspection	Cycloserine Clofazimine
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

A formal documented system of quality assurance was established, with procedures covering all expected key quality elements being in place. The Quality Unit was independent from Production and reported directly to senior management. QA and QC departments were reporting to the Head of the Quality Unit. Operations were specified in written form and GMP requirements were essentially being met. Procedures were in place for notifying responsible management of regulatory inspections, serious GMP deficiencies, product defects and related actions. The procedures that were reviewed and discussed during the inspection were generally of a satisfactory standard. The manufacture of APIs and their intermediates was monitored and controlled, and these results were considered during batch release. Management review meetings were conducted in accordance with a written procedure.

During the opening meeting the company informed the inspectors of the discontinuation of Sofosbuvir API and Terizidone API production and the termination of contract manufacturing for these APIs.
The two APIs had not been manufactured for the last 4 years. The inspectors were informed that Cycloserine and Clofazimine APIs had not been manufactured during the pandemic. Production of these APIs was resumed in 2023.

Quality Risk Management

Quality Risk Management was integrated in the Quality Management System of the company and applied to all production and quality control activities. According to the company's relevant SOP the level, formality, and documentation of the QRM process had to be commensurate with the level of risk. FMEA was used as the tool of choice to conduct risk assessment, but other tools could also be used. Examples of risk assessments were reviewed.

Deviations

Deviations were handled by the QA department according to the procedure "Handling of Deviations". Initially, all events were recorded by the QA department on a template and then were classified as either incidents (not violating an approved procedure and not having a negative impact on product or process) or as deviations (from an approved procedure or process). Deviations were classified as critical, major, or minor, according to the quality impact and GMP violation. Then an investigation was performed to identify possible root causes. An impact assessment was carried out, and CAPAs were identified. Repeated minor deviations were handled as major. The deviations registries for 2022 and 2023 were reviewed along with examples of deviation handling

CAPA

CAPAs were handled according to a written procedure. CAPAs were proposed by the department that was involved in the investigation and the CAPA plan was reviewed and monitored by the QA department. Following CAPA implementation, an effectiveness check was performed and CAPA were either closed out or, in the case of non-satisfactory results, a new round of CAPA was initiated. Finally, there were provisions in place for the extension of the target date for CAPA completion, following appropriate justification and approval by the QA department. A registry of CAPAs by year was maintained. The 2022 and 2023 registries were reviewed. Examples of CAPAs, their monitoring, implementation and effectiveness check were reviewed.

Batch release

There was a procedure in place for certifying and releasing API batches. For API batches intended for the Korean market or supervised by MFDS, the release was performed by the authorised person-legal pharmacist based on BMR and analytical record review performed by the QA department. However, intermediates and APIs intended for overseas markets were released by the QA Head. Release was performed by using a checklist. The person performing the release relied on the QA review and approval of BMR and analytical records. The process also included a verification of the label information attached on containers, the quantity of safety seals used on API containers and the CoA.

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

2. Personnel

The company had sufficient number of personnel with the appropriate education and qualifications to carry out all GMP related activities on-site. Personnel met during the inspection appeared to have knowledge of GMP principles.

Organization charts were in place depicting the administrative and operational reporting hierarchy. Organization charts for different ST Pharm divisions were reviewed, (i.e., QA division, QC1 division, Production 2 division, Logistics division).

Job responsibilities for key personnel were adequately described in job descriptions. Job descriptions were issued and reviewed according to SOP "Management of Job Description" STHA-010(05) and included detailed description of the duties and appropriate qualification. The job descriptions of the QA Team Leader, Production Team Leader and QC Team Leader were reviewed along with the acceptance of duties by the relevant incumbents.

Induction training was initially provided at the time of recruitment and continuous training was provided afterwards based on training needs including but not limited to hygiene, GMP principles, and safety. Training followed the principles described in an SOP. The QA team was responsible for training new employees and a training matrix was used to cover both general GMP topics and job specific duties. The training plan was documented on a template and was approved by QA. For existing personnel two training plans were prepared annually, in December for the next year, describing the training topics. The first plan included general topics and was approved by QA and the second training plan was specific for each department and was approved by the team leader and QA. The QA department was responsible for monitoring the training process. Both training programs for 2023 and their implementation were reviewed. Training was performed by qualified trainers and the list of trainers was made available. Training evaluation was performed by written tests, and relevant records were presented.

Medical examinations followed the principles defined in the procedure. Prospective employees had to undergo a medical checkup before being hired. Employees exposed to higher risk had to undergo medical examinations annually, while for the rest of the personnel, medical checkup was scheduled every other year. Medical examinations were also applicable to temporary workers. Personnel had to complete a health declaration before entering the facilities daily. In case of illness, operators were excluded from production activities. Principles of personal hygiene were described in detail in a written procedure.

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

3. Buildings and facilities

The campus consisted of several buildings. There was a warehouse for raw materials and a separate warehouse for intermediates and finished products (1st floor intermediates, 2nd floor APIs). Drum solvents were stored in a dedicated building. There was also a tank farm for storage of bulk solvents. The water purification system was housed next to the finished products warehouse. There were 5 commercial scale plants and two pilot scale plants on the campus. Manufacture of the WHO prequalified APIs took place in Plant 5 which consisted of 3 floors. Clofazimine (CFZ) was manufactured in Sector 1 of the 3rd floor and Cycloserine (DCS(2)) in Sector 2. Purification and crystallization steps took place on the 2nd and 1st floor (clean area).

Layouts of the facilities were made available. Layouts for personnel and material flow in the clean area (1st floor) were presented. In general, premises were constructed, designed, and maintained to suit the operations to be carried out, to minimize the risk of errors, prevent the risk of contamination of materials and products, and permit effective cleaning and maintenance.

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

4. Process equipment

In general, production equipment was of appropriate standard and surfaces of product contact were suitable. Reactor systems, and utilities, were installed to allow reflux, distillation and cooling required to make the APIs of interest. 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 and records of preventive maintenance were kept. The maintenance plans for 2022 and 2023 were reviewed. The equipment appeared to be installed in a logical order to facilitate production and reduce the risk of contamination and mix-ups. Spot checks on preventive maintenance records of reactors were made. Nitrogen filters were handled according to a written procedure. Filters were replaced annually and checked for their integrity before installation and after replacement. The SOP for maintenance integrity checks and replacement was applicable to filters and to centrifuge bags. Centrifuge bags were product dedicated, appropriately labelled and used for 7 consecutive batches in a campaign and then changed. Procedures for cleaning and records were presented. Procedures for the setup and operation of production equipment were made available.

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

5. Documentation and records

The company had established a documentation system which was mainly paper-based. The hierarchy was referenced in the QM and quality documents were divided into three levels. The quality manual was assigned on the top level, followed by SOPs (level 2), operational manuals, forms and records (level 3). A standard management procedure for issuing, revising, reviewing, approving, distributing, withdrawing, and archiving documents was in place.

The warehouse stock was managed by the Inventory Management System and records were maintained electronically. Similarly, for analytical data generated by the QC department, LIMS was used. In general, documents were designed, prepared, reviewed, and distributed with care. Batch numbers were assigned according to a written procedure. BMRs were completed contemporaneously.

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

6. Materials management There were written procedures describing the receipt, labelling, quarantine, storage, and handling of materials, as well as procedures for sampling, testing and approval or rejection of materials. A check list was used for the receipt of each batch of material. The checklist was partially populated with the material manufacturer information originating from the Inventory Management System. The procedure for the control and management of APIs was made available. Temperature at the finished product warehouse was controlled and monitored while relative humidity was monitored but not controlled. Minimum and maximum differential pressure limits in the sampling and dispensing areas had not been defined.

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

7. Production and in-process controls In general, production operations followed defined procedures. Process flows and routes of synthesis were available. Access to production premises was

restricted to authorized personnel. 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 examined during the inspection.

The manufacturing of DCS(2) included one reaction step and several purification steps. Manufacturing took place in Sector 2 of Plant 5. The inspectors visited Plant 5 and the clean area where the final filtration, vacuum drying, and packaging were taking place at the time of inspection.

The manufacturing of CFZ included two major synthetic steps and several purification steps before vacuum drying, milling, and packaging. CFZ was manufactured in Sector 2 of Plant 5.

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

8. Packaging and identification labelling of APIs and intermediates

Intermediates were handled, as required, in dedicated containers. Finished products were packed in double bags and protected from light, where necessary, before being placed in their final container. Examples were seen of those used for DCS(2). Finished product containers were appropriately sealed and labelled. Safety seals were used, and the quantity used was recorded. Information on quarantine/under test and release status/labels was verified. Information on finished product labels and number of safety seals used, were reviewed as part of the BPR before final release.

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

9. Storage and distribution

The company had several dedicated warehouses for the storage of solid raw materials, solvents, intermediates, and finished products. There was a warehouse for solid raw materials and a separate warehouse for intermediates and finished products (1st floor intermediates, 2nd floor APIs). Drum solvents were stored in a dedicated building. There was also a tank farm for storage of bulk solvents. Temperature was monitored in all warehouses, except for the tank farm. Relative humidity was recorded but not controlled in the warehouse of intermediates and finished products. Records of incoming material and finished goods were maintained in the Inventory Management System. Only released intermediates and finished products could be dispatched. The principles for storage and distribution were described in a written procedure.

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

10. Laboratory controls

The analytical laboratories were inspected. The premises were generally of an acceptable standard and well equipped. LIMS was used in the laboratory to trace test requests, allocate samples and record test results. Documents were organized in an appropriate manner and retrieval was achieved in a timely manner. Sampling of raw materials took place after registering a request in LIMS. A sampling form was generated including the quantity to be withdrawn. Labels to be affixed on collected samples were pre-printed and included the theoretical weight to be withdrawn from each container. The exact weight was

recorded on the sampling form. An example of sample registration was reviewed. The allocation of the sample to an analyst was registered in LIMS. The sample quantity to be used for each test was recorded and reconciliation was performed.

Laboratory equipment was of appropriate standard. Qualification and validation labels were affixed on laboratory equipment. Logbooks for equipment use were maintained. The logbook for the HPLC columns was reviewed.

The following analytical documentation was reviewed:

- The Sampling Instruction for Cycloserine
- The Specifications and Test Method for Cycloserine
- The Test Method for Cycloserine Related Substances
- The Operation manual HPLC Agilent
- The Consumption Logbook of USP Cycloserine standard
- The Manual integration SOP
- The Empower SOP

Similarly, the following documentation relating to the analysis of Clofazimine API was reviewed:

- The Clofazimine Test Method- Polymorphism
- The Clofazimine Test Method- Residual Solvents

Out of Specification results

Handling of OOS was described in the SOP "Handling of OOS, OOT, and OOE results". If an obvious analytical error was not identified during the initial investigation, a pre-approved hypothesis testing was performed. In the case a root cause was identified, provisions were in place to invalidate the initial test results and retesting was performed. If a root cause was not identified after hypothesis testing, a full investigation was performed according to the SOP "Full scale investigation". The final decision for approval or rejection of the batch was made by the Head of the GMP Committee (QA Director). OOS results were registered, and the relative records were reviewed

Stability

The company had a dedicated area for housing the stability chambers. There were nine stability chambers covering all climatic zone conditions including 2 backup chambers. There was a procedure in place for managing stability samples and an inventory was maintained. Stability samples intended for testing for the first time point of the stability study had to be withdrawn ±3 days of the set dates. Samples for the remaining time points had to be withdrawn ±7days before the set dates. Stability samples were placed in double bags and a PE container was used for secondary packaging.

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

11. Validation

Requalification of the equipment was performed every 5 years according to a written SOP. An extension to the requalification period could be granted following a documented risk assessment. Examples of production equipment qualification were reviewed.

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

12. Change control

The change control procedure provided guidance on the management and implementation of changes which was applicable to amendments including but not limited to changes related to the production process, equipment, utilities, facilities, materials, and systems. The change relating to the replacement of the PW system was reviewed along with relevant documentation:
The Site Acceptance Test -IQ
The Phase I Qualification of the Water Generation System
The Phase II Qualification of the Water Generation System

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

13. Rejection and re-use of materials

The company had in place a procedure for the return of APIs. The same procedure included instructions for rejecting non-conforming materials, intermediates, and finished products.

The procedure for "Reprocessing / Reworking was reviewed. Definitions for reprocessing and reworking were included in the procedure. The final approval for reprocessing / reworking was granted by the QA department. Further testing and a stability study of the reprocessed/reworked finished product were foreseen. Reprocessed/reworked batches were assigned new batch numbers. An example of a reprocessed batch was reviewed

A procedure for the recovery of ethanol used in the DCS(2) manufacturing process was available. The recovery was performed by ST Pharm and the purification was carried out by a contractor. Specifications for the purified ethanol were established and a risk assessment on the recovery of ethanol had been performed. The recovered solvent could only be used for the same process step in DCS(2) synthesis.

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

14. Complaints and recalls

The company had in place a procedure for handling complaints. Complaints were usually received by the QA Team or the New Drug Development and Innovation Department or the Business Division. They had to be registered within 24 hours of receipt and investigations had to be completed within 30 days. A further 30-day extension could be granted based on appropriate justification. Recurrence of complaints was checked by QA and a review was performed every six months. The complaint report for the first half of 2023 was presented. The areas reviewed included the nature of complaint, root cause investigation, measures/CAPA, number of batches affected and time for closing out the complaint. No complaints had been received.

A procedure for recalling defective products/batches from the market was in place. A recall could be decided either by regulatory authorities or by the GMP Committee. Recalls were classified in three categories based on risk and impact. There was a provision to conduct mock recalls if the previous two years no recall was conducted. The Cycloserine mock recall conducted on 20.08.2021 was reviewed and discussed.

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

15. Contract manufacturers (including laboratories)

Ethanol from the DCS process was recovered and purification was carried out by a contractor. The latest assessment and requalification of the contractor was performed in January 2023 based on a quality related questionnaire completed in November 2022 and an on-site audit carried out the same month. The audit response was provided by the contractor in April 2023. The original technical agreement with the contractor was made available

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

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, ***ST Pharm Co. Ltd. (Sihwha)***, located at ***231 Hyeomnyeok-ro, Siheung-si, Gyeonggi-do, 15086 Republic of Korea street,*** 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-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. 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.
Short name: WHO TRS No. 992, Annex 5
https://www.who.int/publications/m/item/trs992-annex5

21. WHO Recommendations for quality requirements when plant – derived artemisinin is used as a starting material in the production of antimalarial active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 6.
Short name: WHO TRS No. 992, Annex 6
https://www.who.int/publications/m/item/trs-992-annex-6

22. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4.
Short name: WHO TRS No. 1033, Annex 4
https://www.who.int/publications/m/item/annex-4-trs-1033

23. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
Short name: WHO TRS No. 996, Annex 10
https://www.who.int/publications/m/item/trs966-annex10

24. 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***
https://www.who.int/publications/m/item/trs1010-annex10

25. Points to consider when including Health-Based Exposure Limits in cleaning validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 2.
Short name: WHO TRS No. 1033, Annex 2
https://www.who.int/publications/m/item/annex-2-trs-1033

26. 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
https://www.who.int/publications/m/item/trs-1025-annex-6

27. Production of water for injection by means other than distillation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 3.
Short name: WHO TRS No. 1025, Annex 3
https://www.who.int/publications/m/item/trs-1025-annex-3-water-for-injection

27. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4.
Short name: WHO TRS No. 1025, Annex 4
https://www.who.int/publications/m/item/trs1025-annex4

28. Good trade and distribution practices for pharmaceutical starting materials. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 6.
Short name: WHO TRS No. 996, Annex 6
https://www.who.int/publications/m/item/annex-6-trs-996

29. WHO guidelines for preparing a laboratory information file. *WHO Expert Committee on Specifications for Pharmaceutical Preparations.* Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 13.
Short name: WHO TRS No. 961, Annex 13
https://www.who.int/publications/m/item/trs961-annex13

30. WHO good manufacturing practices for excipients used in pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-seventh Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052), Annex 1.
Short name: WHO TRS No. 1052, Annex 1

https://www.who.int/publications/i/item/9789240091030