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 Unit Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Finished Product Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**S Kant Healthcare Limited**
Corporate address of manufacturer	3-A, Shivsagar Estate, Dr. A Besant Road, Worli, Mumbai - 400 018. Tel.: +91 226622 7575 Fax: +91 226622 7500 Email: skhl@sk1932.com
Inspected site	
Name & address of inspected manufacturing site if different from that given above	1802-1805, GIDC, Phase III, Vapi, 3961195, Gujarat, India D-U-N-S Number: 918311416 Co-ordinates: 20.364728, 72.946663 and (20°21'53.0"N 72°56'48.0"E)
Unit / block / workshop number	Oral Solid Dosage form section
Inspection details	
Dates of inspection	15-19 November 2021 13-16 June 2022
Type of inspection	Routine cum-follow-up GMP inspection
Introduction	
Brief description of the manufacturing activities	Manufacturing and quality control of active pharmaceutical ingredients (APIs) and non-sterile oral solid dosage products (FPP).
General information about the company and site	S Kant Healthcare Ltd. was established in the year 1996. The site is located at 1802-1805, Phase Ill, G.I.D.C., Vapi, 396195, Gujarat India. At this location there are two separate manufacturing sites, one is a bulk drug and another one is a formulation. The formulation Plant is equipped for the formulation of General Products (non-beta-lactam) in different dosage forms viz., Solid Oral Dosage Form (Tablets, Capsules & Dry Syrup), Liquid Orals Dosage Form (Suspension & Syrup), Semi-Solid Dosage Form for Topical Application (Ointments, Gel & Creams). The API site produces Artemisinin bases like Artemether, Artesunate, Dihydroartemisinin and Lumefantrine.
History	This was the third WHO PQ inspection on S Kant Healthcare Limited. The site was previously inspected in March 2019 and in November 2021. Further to this, the manufacturing site was inspected by the National Medicines Regulatory Authorities from several African countries including the NRA of Malta.

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	The follow-up inspection was limited to the verification of CAPA.
Restrictions	None
Out of scope	The FPPs under the scope of WHO Prequalification were inspected. The rest of the products including APIs were out of the scope of this inspection.
WHO products covered by the inspection	1. MA144 Sulfadoxine/Pyrimethamine Tablet, Dispersible 250mg/12.5mg 2. MA145 Sulfadoxine/ Pyrimethamine Tablet, Dispersible 500mg/25mg 3. MA146 Pyrimethamine/Sulfadoxine + Amodiaquine (hydrochloride) Tablet, Dispersible 12.5mg/250mg + 75mg 4. MA147 Pyrimethamine/Sulfadoxine + Amodiaquine (hydrochloride) Tablet, Dispersible 25mg/500mg + 150mg
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
APS	Aseptic process simulation
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CFU	Colony-forming unit
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
GPT	Growth promotion test
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
LAF	Laminar airflow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae

MFT	Media fill Test
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
SIP	Sterilization in place
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer
WFI	Water for injection

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

1. Pharmaceutical quality system

The company has established a quality management system (QMS) based on the requirement of national and international regulatory authorities. The quality and production departments operate independently under different leadership. Since the last WHO PQ inspection held in November 2021, the Senior Management had demonstrated a commitment to the QMS by implementing various systems and processes to bring up the level of PQS. The following elements of PQS were reviewed:

Quality Excellence Program

The management team under the direction of the Associate Director have developed a comprehensive plan to target and sustain the achievement of Quality Excellence by all staff continuously. The level of commitment by the Directors of the Company and the management team was evident throughout. The program commenced on 20/5/2022 with a "Town Hall" meeting attended by all staff and management at which a presentation summarizing the objectives and high-level timelines were communicated. The program is well designed and includes a multi-faceted approach to achieve a range of objectives which will require both internal and external facilitators.

Data Integrity

As part of the "Quality Excellence Program", a Data Integrity Policy was published by the Associate Director in charge of the Manufacturing Site which was supported by a series of "mind maps" and information posters which were visible throughout the facility.

Management Review

Management Review (MR) was conducted twice per year as per the procedure. The procedure defines the objectives of the meeting and the responsibilities of Senior Management in reviewing and commenting on the effectiveness of the PQS.

Quality Risk Management

Quality Risk Management (QRM) was performed according to the procedure which states that although the default QRM tool for risk assessments (RA) is Failure Mode Effects Analysis (FMEA), the additional tools of Failure mode, effects and criticality analysis (FMECA), Fault Tree Analysis (FTA), Hazard analysis and critical control point (HACCP), Hazard operability analysis (HAZOP), Preliminary Hazard Analysis (PHA) and Diagrammatic methods should be considered based on the application. The SOP was supported by Annexure which contains a detailed FMEA outline together with the numerical rating system used to calculate the risk priority number (RPN) both before and after the implementation of risk mitigation actions.

Deviations and Incidents

Based on the list of deficiencies raised during the last WHO PQ inspection, the company had raised several incidents. The procedure for handling deviations was revised.

Change control management

The SOP on the handling of change control was reviewed. The revision was made based on the deficiency raised during the last WHO PQ inspection. The annexure-VIII on risk management evaluation for the new product/molecule introduction was added.

Product Quality Review

The updated SOP for Product Quality Review was reviewed to confirm if previously identified shortcomings had been addressed. The staff interviewed were confident in their subject and showed the sections of the SOP which had been updated i.e. inclusion of all products even if not produced, the justification for the number of batches required before the trending of yields, the use of a validated application for calculating the process capability index (Cpk) a log of Cpk values calculated per parameter with a two-person verification to ensure those investigations were initiated whenever Cpk values were below 1.00 or between 1.00 and 1.33.

The deficiencies noted from the pharmaceutical quality system section have been addressed satisfactorily and the same will be verified during future PQ inspections.

2. Good manufacturing practices for pharmaceutical products

The follow-up GMP inspection verified the CAPA implemented since the last WHO PQ inspection was held in November 2021. Based on the visit to the production and packaging areas, it was evident that the site has made several changes in its layouts and created new common airlocks (personnel and material) in some core processing areas. The granulation areas and compression areas now have the same procedure and airlock availability. In addition, the manufacturer had implemented some closed systems for the transfer of materials and in-process materials. Similarly, the procedures and controls for packaging areas have been completed.
The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

3. Sanitation and hygiene

Premises and equipment were generally cleaned according to established procedures. Change rooms were maintained and authorized instructions displayed the steps and dress code. The gowning practice has been changed from every three days to every day.

4. Qualification and validation

The qualification and validation programs were designed to evaluate the manufacturing process and process equipment to assure quality and cGMP compliance. Qualification programs for area and equipment were performed periodically to ensure the suitability of the area and equipment. Validation programs were established to verify and document the ability to attain reproducible results during manufacturing, packaging, testing, and cleaning operations. Since the last PQ inspection, the company has performed the cleanability study
The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

5. Complaints

The complaint handling procedure was revised and now the procedure describes the 6xM methodology for establishing and documenting the root cause investigation of complaints. The procedure has been cross-referenced with the QRM procedure. There were no complaints recorded for WHO products since the SOP update. A recent product complaint investigation was reviewed which confirmed that the new requirements were applied.

The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

6. Product recalls

The SOP for Product recall refers to an updated Mock recall Protocol. Section 7 of the records for the mock recall contains comprehensive details for the reconciliation of quantities which was included in the "Evaluation & Summary" section of the document.
The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

7. Contract production, analysis and other activities

The company did not employ contract production and packaging activities for WHO PQ products. The company uses contracted laboratories for testing elemental impurities and other tests where facilities were not available on-site.

8. Self-inspection, quality audits and suppliers' audits and approval

Internal audit (Self Inspection) SOP was updated and now included a specific reference for the review of compliance to DI as per the ALCOA+ principles. This was confirmed during the review of the internal audit checklists for engineering and the secondary packaging floor. The minutes of the Management Review meeting recorded that all internal audits had been completed and closed as per plan as well as a review of the status of audit responses for all "external" audits of the facility (including WHO).

The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

9. Personnel

The company employed 263 personnel for carrying out various manufacturing operations for non-sterile OSD products as well as other products manufactured on-site. A change control about the revision of the site organogram was reviewed. The change was raised by the Associate Director, Harshit Shah. The proposed change was to create a new position "Site Technical Head" who will oversee day to day operation of the site and is also responsible for administrative reporting (attendance, safety and disciplinary issues) from QA Heads. A draft organogram was prepared and the proposed reporting structure confirmed the separation of operations and QA functions. The company need to draft a job description for the new position and confirm the timeline for when this new position will be filled.

<u>GMP Consultant</u>
An agreement between S Kant and a consultant was reviewed. The agreement stated the scope of the work including a nondisclosure agreement covering confidential information. The CV of the consultant was in place. From the information provided in the CV, the consultant had the relevant qualification and work experience to be a pharmaceutical consultant.
The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

10. Training

Training of Plant Personnel was performed following SOP on the training of personnel. The head of human resources was responsible for training and the retention of training records and worked in close collaboration with the head of Quality. The procedure outlines a common approach for all new permanent staff starting with a 7-day induction program via a combination of personal instruction, self-study and classroom training under the guidance of the supervisor. Once the supervisor has approved the satisfactory completion of induction, the staff member is required to serve a further one-month period during which they receive further on-the-job training while their performance is closely monitored. On completion of this program, the staff member is certified as competent for the agreed job function.

A matrix of the SOPs required per job specification was available from which the annual Training need identification for 2022 was prepared which included annual cGMP training, on-the-job, SOPs and SOP refreshers, safety, external, incidental and classroom training formats. The 2022 training plan consisted of 36 original modules plus an additional 11 modules in response to the WHO audit.

The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

11. Personal hygiene

The personnel gowning procedure was appropriate and was generally followed. It was noted that gowning was changed from once every three days to daily.
The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

12. Premises

The inspector visited the premises and verified that the diesel generator (DG) was installed outside of the main DG set. It is a fixed structure and rented for 3 years.

The inspection team visited the scrap yard and improvements were noted from the last WHO PQ inspection. Separate locked areas were provided for the storage of expired medical products and out-of-specification products. The antimicrobials should be carefully handled (Bharuch Pollution Board incinerate expired products). Visited tablet production and packaging areas. The improvement has been made since the last PQ inspection in the production and packaging areas.

The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

13. Equipment

The equipment used in the manufacturing, processing, and packaging was of appropriate design. The equipment was placed in a suitable location to facilitate operations for their use, cleaning, and maintenance.

Data Integrity risk assessments for 124 and 102 types of equipment within the solids production and packaging areas respectively have been completed according to the "DI RA protocol cum Report for applicable Instrument/Equipment or System". The evaluation and the results of each ALCOA+ element for both electronic and/or paper-based controls were recorded in an "Annex 1" document for each type of equipment. The DI risks identified were then recorded and actioned as described in section 1.2 of this report.
The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

14. Materials

The SOP for the sampling of packaging material has been significantly improved to ensure that the correct number of containers are sampled and that containers that have been sampled are easily identified. The Pharmacloud system now includes a module which automatically calculates the number of samples required and generates the same number of a new sampling label which contains all of the required information and a space for the signature of the sampler. The labels are affixed to the sampled containers by QC after which the details are reviewed by a second person. The implementation of this system as well as a new sealing tape for sampled containers containing the words "SK QC Sampled" was confirmed during a visit to the materials warehouse.

The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

15. Documentation

In general, documentation was designed, prepared, reviewed, and distributed according to a documented procedure. Quality system documents were regularly reviewed and kept up to date. Approved, signed and dated testing procedures and specifications were available for starting and packaging materials and for finished products.

The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

16. Good practices in production

Clean areas for the manufacture of non-sterile OSD products were classified (ISO 8) according to the expected required characteristics of the environment. Separate change rooms were provided for visitors and staff members.

Changes have been made in the production areas, and common airlocks (personnel and materials) were created before entering into the core processing areas. The Granulation areas and compression areas now have the same procedure and airlock availability. Similarly, closed systems (transfer of materials and in-process materials) were incorporated in some areas and work is in progress.
The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

17. Good practices in quality control

Data Integrity risk assessments
Data Integrity risk assessments for all the equipment listed in the Chemistry and Microbiology laboratories have been completed according to the "DI RA protocol cum Report for applicable Instrument/Equipment or System". The evaluation and the results of each ALCOA+ element for both electronic and/or paper-based controls are recorded in an "Annex 1" document for each type of equipment. The DI risks identified were then recorded and actioned as described in section 1.2 of this report.

Shimadzu HPLC's running on LabSolutions Software.
The DIRA's for this equipment raised 4 separate risks all of which related to the electronic signature function not being enabled. The mitigation factors were based on the current practice of printing hard copies of all chromatograms, method tables, results tables, warning logs and audit trails for review by the supervisor who physically signs on the documents concerned. A review of the analytical raw data for the assay of batch WSA 21053 of Sulfadoxine and Pyrimethamine Tabs Dispersible (AR number SKF2091/21) confirmed each of the manual signature points identified in the DIRA. The validation of the Excel-based software application used in the assay calculation (refer to section 4.1), as well as the confirmation of the data transcribed from the worksheets to the Pharmacloud system for the generation of the final COA, were also reviewed and found to be in order.

UV Shimadzu QC/137 and QC/154 (confirmed same software version).
The DI RA for this equipment was essentially the same as for the HPLCs above with the lack of the electronic signature function being replaced by physical checks and signatures of printed outputs.

GMP Model Vertical Autoclave QM/025
The DI RA for this equipment confirmed that there are no computerized controls in place but that the requirements of ALCOA+ are achieved entirely via the review of the printout of key set points and achieved values together with manual logbooks for the associated metadata. The only medium-term CA listed was to evaluate the upgrading of the current control systems.

QM/026 Volumetric Air sampler for viable counts
The DI RA for this equipment confirmed that there are no electronic controls in place but that the requirements of ALCOA+ are achieved entirely via the review of the printouts of sampling sheets and manual logbooks for the associated metadata. The only medium-term CA listed was to replace these units with embedded ALCOA+ compliant versions.

Administration for granting rights to operators and developers

Following the observations made in the previous audit, the laboratory instruments administrator received training from the supplier of the LabSolutions software before updating the SOP for User Management and Security Policy of the Labsolution Server/ ACQ (Client) System. The system is now separated into 7 groups with the role of the reviewer separated from the other groups. The role of QC Manager has been reserved for the performance of manual integrations with the rights to this role only given for a defined period to allow for completion of the reintegration as per the instructions to the administrator recorded in the associated deviation. Annexure 5 governs the process used to verify the allocation of roles and responsibilities for all laboratory systems on a 6 monthly basis. Records of this activity were reviewed and found to be systematic and complete

Manual Integration

As described in section 17.2 above, no users have been allocated permanent rights to perform manual integration. The conditions under which manual integration may be considered are included in the "Chromatographic Technique" which requires the process to be authorized and recorded in a deviation. Section 5 of the procedure includes a detailed list of typical manual integration examples with suggestions on how to manually integrate as well as instructions on calculations, data review and data storage.

Allocation of work within the Quality Control Laboratories

The Procedure for Work distribution requires the laboratory supervisors to check that an analyst is competent in a specific technique before allocating the work and that the analysts confirm the same. The competency matrix and records of this allocation were reviewed and found to be in order.

Laboratory glassware washing

Change control for the installation of a glassware washing machine (Lab India Smart washer M2) in the chemistry laboratory was reviewed which included the requirements for equipment qualification starting with a URS, IQ&OQ and PQ. The SOP describes the various programs and loading patterns which were understood by the operator interviewed during the laboratory inspection.

Validation of the cleaning cycles was summarized in the executed report. The validation used Erythromycin Stearate as the worst-case marker based on solubility and included quantitative analysis of analyte concentrations prior to and after washing all of which compared to the acceptance criteria

The effectiveness of SOP for "Washing and Cleaning of Glassware in microbiology laboratory" SOP was validated using a series of positive and negative controls for 4 organisms. The study was well executed with all results complying with the acceptance criteria.

The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future 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, ***S Kant Healthcare Pvt Ltd***, located at ***1802-1805, GIDC, Phase III, Vapi, 3961195, Gujarat, India*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines.

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://digicollections.net/medicinedocs/documents/s21467en/s21467en.pdf

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***
   untitled (digicollections.net)

3. 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
   9789240020900-eng.pdf (who.int)

4. 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://digicollections.net/medicinedocs/documents/s21440en/s21440en.pdf

5. 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://digicollections.net/medicinedocs/documents/s23455en/s23455en.pdf

6. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4.
Short name: WHO TRS No. 937, Annex 4
https://digicollections.net/medicinedocs/documents/s20108en/s20108en.pdf

7. 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. 961, 957), Annex 1
https://digicollections.net/medicinedocs/documents/s18681en/s18681en.pdf

8. 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://digicollections.net/medicinedocs/documents/s22358en/s22358en.pdf

9. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 6.
Short name: WHO TRS No. 961, Annex 6
https://digicollections.net/medicinedocs/documents/s19959en/s19959en.pdf

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7.
Short name: WHO TRS No. 961, Annex 7
https://digicollections.net/medicinedocs/documents/s18677en/s18677en.pdf

11. 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://digicollections.net/medicinedocs/documents/s18683en/s18683en.pdf

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://digicollections.net/medicinedocs/#d/s21438en

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://digicollections.net/medicinedocs/documents/s18682en/s18682en.pdf

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://digicollections.net/medicinedocs/#d/s20177en/

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://digicollections.net/medicinedocs/#d/s20175en/

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
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

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://digicollections.net/medicinedocs/documents/s23697en/s23697en.pdf

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***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

19. 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***
Essential Medicines and Health Products Information Portal (digicollections.net)

20. WHO Recommendations for quality requirements when plant – derived artemisin 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/who-recommendations-for-quality-requirements-when-plant-derived-artemisinin-is-used-as-a-starting-material-in-the-production-of-antimalarial-active-pharmaceutical-ingredients---trs-992---annex-6

21. 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***
9789240020900-eng.pdf (who.int)

22. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
Short name: WHO TRS No. 996, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

23. 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
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

24. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditionning 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://digicollections.net/medicinedocs/documents/s23699en/s23699en.pdf

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**
9789240020900-eng.pdf (who.int)

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** 9789240001824-eng.pdf (who.int)

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-detail/978-92-4-000182-4

28. 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-detail/978-92-4-000182-4