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

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**Steril-Gene Life Sciences Pvt Ltd**
Corporate address of manufacturer	No.15, Gopalakrishnan Road T-Nagar Chennai India 600017
Inspected site	
Name & address of inspected manufacturing site if different from that given above	No. 45 Mangalam Main Road Mangalam Village Villianur commune Puducherry 605110 India
Unit / block / workshop number	Block C
Inspection details	
Dates of inspection	13 to 17 June 2022
Type of inspection	Initial on-site inspection
Introduction	
Brief description of the manufacturing activities	Production, quality control and distribution of tablets, capsules (hard and soft gelatin), injectables (including lyophilized). Hormone and high potent products are produced on the site.
General information about the company and site	The manufacturing site of Steril-Gene Life Sciences (P) Ltd. manufactures both human and veterinary medicines. The site has several independent manufacturing blocks. Penicillin group products and cytotoxic products were not manufactured on site. Block C is not dedicated to production of Oxytocin sterile injection products. Both aseptic and terminal sterilization products shared the facility and production lines.
History	The current inspection was the first on-site inspection after the product manufacturing site being accepted by WHO medicines PQ programme based on the desktop review held in June 2019.

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	• Quality management system • Injectable Production Block C • Quality Control laboratories: Physical, chemical and microbiology labs • Utilities: Water and Nitrogen system • Warehouses
Restrictions	The inspection was restricted to the production of the product listed in the inspection scope.
Out of scope	All other products and production facility on the site were outside of the inspection scope and were not visited.
WHO products numbers covered by the inspection	RH083 Oxytocin Solution for Injection 10 IU/ml
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 air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae

MFT	Media fill Test
MR	Management review
NC	Non conformity
NCA	National control authority
NCL	National control laboratory
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
PUPSIT	Pre-Use Post Sterilization Integrity Testing
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RABS	Restricted access barrier systems
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 (where applicable)**

1. Pharmaceutical quality system

A documented system for quality assurance was established, with procedures covering key quality elements in place. Operations were specified in written form and critical GMP requirements were essentially being met. The procedures reviewed and discussed during the inspection were generally of an acceptable standard. The Quality Department was divided into QA and QC and were independent from Production.

Annual Product Quality Review (PQR)

SOP for Product Quality Review was reviewed. PQR was required to be prepared from January to December of the year for review and the compilation was to be completed before the end of March of the subsequent year.

Oxytocin Injection BP 10 IU/ml has two production batch sizes. APQR for Oxytocin Injection BP 10 IU/ml approved in the year of 2021 and 2022 were reviewed. Change control, deviation, complaint, OOS and batches rejection etc. were reviewed. No product recall and product complaint occurred in the review period.

Quality Risk Management

Quality risk management and risk assessment was managed and performed according to SOP for Quality Risk Assessment. Various approaches to risk assessment were allowed, but the focus was on utilization of the FMEA model. Several quality risk assessments were reviewed during the inspection.

Management review (MR)

Quality management review was managed according to a written SOP. A MR meeting minutes dated in April 2022 and the presentation prepared for the meeting were reviewed and found to be generally acceptable.

Change control (CC)

SOP for change management was available for review. The procedure was applicable to both permanent and temporary changes and classified as major or minor. The scope of the change management, time period for closure and effectiveness of CC implementation were stipulated in the procedure. CC logbook and several CCs were reviewed and discussed during the inspection.

Deviations

SOP for Deviation Management was checked and found to be generally acceptable. The procedure described the processes for reporting, assessing, investigating, implementing, and closing of a deviation which occurred during the manufacturing activities or processes that impact on the quality and/or compliance of the product, systems, services, GMP and facility. 2020 and 2021 Logbooks for Deviation were available and checked. Several deviations including reporting, investigation and CAPAs were checked during the inspection.

CAPAs

SOP for Corrective and Preventive Action applied to any quality and GxP non-compliant issues, risks or recommendations for action identified for activities or processes that could impact the quality and/or compliance of products, systems, services, or studies. CAPAs required for product recalls, customer complaints, deviations, OOS, OOT, lab deviations, inspections by regulatory authorities, audits and self-inspections, quality systems review and product quality reviews. CAPAs closed according to the proposed target date. The effectiveness of the CAPA was required to be monitored. Checked Logbooks for 2020 and 2021 for Block C.

OOS and OOT

SOP for Investigation of Out of Specification Results was reviewed and found to be generally acceptable. An OOS resulted in batch rejection in 2021, related OOS investigation and CAPA was reviewed.

Batch numbering system

SOP for Allocation of Batch Number, Manufacturing and Expiry Date and SOP for Production batch plan change / Batch cancellation form for Oxytocin Injection BP 10IU /ml were reviewed and discussed.

Product release

FPP batch release was managed according to an approved SOP. The procedure reviewed was generally of an acceptable standard.

2. Good manufacturing practices for pharmaceutical products

Good manufacturing practices were generally implemented. Necessary human and physical resources with premises, equipment and utilities were provided for the current operational level of Oxytocin Injection manufacturing activities. The manufacturing processes followed procedures as defined and documented in the BMRs.

3. Sanitation and hygiene

Premises and equipment in the FPP production area were maintained at a satisfactory level of cleanliness at the time of inspection. Sanitation of clean areas is performed frequently in accordance with the SOP. Personal hygiene and sanitation with appropriate hand washing facility appeared satisfactory. The facilities for sanitation and hygiene established on the site appeared acceptable.

4. Qualification and validation

Validations and qualifications performed according to the site policy, validation master plan, and documented procedures. Process validation and equipment qualification identified what qualification and validation activities were required. The key elements of a qualification and validation programme were defined. Media fill for the production line in Block C performed every six months. Critical equipment was requalified as per documented schedule, however, PUPSIT was not equipped in the production line at the time of inspection. A CAPA has been addressed to the deficiency with a timeline for implementation.

Process validation and Media fill

- SOP for Validation Master Plan
- SOP for Process Validation
- Process Validation Protocol and Summary Report for Oxytocin Injection BP 10 IU/ml for increased batch size with three validation batches
- Executed BMRs for Oxytocin Injection BP 10 IU/ml
- SOP for Aseptic Process Simulation Programme (Media Fill)
- Media Fill Protocol and Summary Report
- Media Fill Executed BMRs
- Sterile Area Authorized Personnel List 2021 and 2022

- Block C Area Classification
- Smoke test of filling LAF validation and documented in video
- Protocol and Summary Report for Fogging Validation in Block-C
- Test Request Format for Fogging Validation in Block-C

Equipment

- Requalification Protocol Summary Report for Bung Processor Cum Steam Sterilizer
- Performance Qualification Protocol and Summary Report for Cold Room

Utilities

- Nitrogen generation plant layout
- Performance Qualification for Nitrogen Gas Generation and Distribution System

Cleaning validation

SOP for Cleaning Validation was available for review. Due to time constraints in the inspection, it was not covered in depth.

5. Complaints

SOP for Handling Market Complaints was reviewed. Checked Logbook for Market Complaint Register for Block C. No complaints for Oxytocin recorded in 2021.

6. Product recalls

SOP for Product Recall reviewed and found to be acceptable. No recall history for this product at Steril-Gene. Mock recall was required to be performed every 2 years. A mock recall performed in 2020 was concluded successful.

7. Contract production, analysis and other activities

The company did not contract out any manufacturing.

SOP for Selection, Audit, Approval and Regularization of Contract Testing Laboratories was reviewed. Approved contract laboratories were used for the analysis of raw materials.

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

Self-inspection

SOP for Self-Inspection was reviewed. The QA Head identified experienced and qualified auditors. The self-inspections conducted using a checklist for the respective departments. The results of the self-inspections recorded on an approved template. The necessary CAPAs initiated, as required and effectiveness checks performed. No critical observations were noted during the 2021 self-inspection.

Vendor approval

SOP for Vendor Qualification and Approval was reviewed. The procedure covered the identification, evaluation, qualification, re-qualification, approval, and disapproval of a vendor.

The following was checked for Oxytocin API EP (Injectable Grade):

- Supplier Qualification
- Quality Technical Agreement
- Initial approval
- Requalification

The following was checked for glass ampoule USP Type-1:

- QA for Packaging Material Approved Vendor List
- Approved vendors for primary packaging material (glass ampoule USP Type-1)

9. Personnel

There was adequate number of personnel suitably qualified by education and training to perform and supervise the manufacture of FPPs. The personnel met during the inspection appeared to be knowledgeable about GMP. An organization chart and key personnel responsibilities, including site VP-Operations, QA Head and QC Head were reviewed.

10. Training

SOP for Employee Training was reviewed and found to be generally acceptable.
Checked the following:

- Annual training schedule for Block C: Microbiology
- Training Record and Evaluation Sheet for Aseptic Area Behaviour (2021) for employees

11. Personal hygiene

Changing and hand washing before entry to production areas followed company procedures.
Direct contact avoided between the operator's hands and starting materials, primary packaging materials and intermediate or bulk product. Staff observed in critical areas dressed in appropriate protective clothing.

12. Premises

The site consists of several independent production blocks. The injection production line used to produce Oxytocin Injection 10 IU/ml was in Block C.

Changing rooms designed as airlocks and used to provide physical separation of the different stages of changing. Changing rooms flushed with filtered air. The final stage of the changing room was in the at-rest state, the same grade as the area into which it leads.

QC laboratories were separated from production areas. QC Laboratories were located in two different blocks.

A centralized warehouse on the site was used for the storage of general category API and excipients, packaging materials and FFP. Cold storage was used to store Oxytocin API and FPP at 2 °C to 8 °C. Cold storage of the FPP is a Walk-In Cold Room within the warehouse.

Utilities

Adequate ventilation, air filtration and exhaust systems provided. The HVAC system providing filtered air to the cleanrooms. The particle count deviation observed in APQR.

Nitrogen used for production process generated on site. The nitrogen system was briefly visited. The change control and qualification documentation were reviewed during the inspection.

Water System

Purified water produced from bore well water by double ROs followed by EDI. Water for injection (WFI) was produce by distillation method. The PW and WFI system were visited and spot checked for the operational parameters. No objectional comments made.

13. Equipment

There were two manufacturing lines and two packaging lines available in Block C. One of the two filling machine used for Oxytocin Injection 10 IU/ml production was inspected. The product filling line was equipped with open RABS as a barrier for human interventions during the aseptic filling. The gloves had been installed on the RABS. The filling machine setup was observed during the inspection.

After sealing, filled ampoules were collected, and transferred out of filling room for inspection. The labelling process was performed using labelling equipment followed by manual check and manual secondary packaging operation.

14. Materials

Block C had a dedicated area for quarantine and approved materials. Sampling was performed by QC in sampling booths.

SOP for Handling of Returned, Rejected and Expired Finished Goods was available for review. Expired finished goods were required to be identified through the ERP. Rejected finished goods were identified by a "Rejection Note". Rejected/Expired finished goods were required to be transferred to the Rejection Area and kept under lock and key with the appropriate status label.

15. Documentation

The documentation system was paper based and controlled by QA department. In general, documentation designed, prepared, reviewed and distributed according to documented procedures. Documents reviewed every 2 years.

16. Good practices in production

WHO grade Oxytocin Solution for Injection 10 IU/ml prequalified in 2019 based on a desktop review. This was initial WHO onsite GMP inspection. The production of Oxytocin Solution for Injection 10 IU/ml was in operation during the week of this inspection. The Block C production area inspected from CNC corridor.

The Clean areas for the manufacture of sterile products were classified according to the environment requirement for aseptic production process. The filling line used for WHO Oxytocin Injection was non-dedicated and shared with terminal sterilized injection products including solution for injection and lyophilised powder for injection products. The material dispensing, machine setup, filling and packaging operation observed at the time inspection. The operations found acceptable in general, however, some weakness noted and require improvements which have been addressed in CAPA at a satisfactory level.

17. Good practices in quality control

There were two QC laboratories on the site. The QC laboratory was well equipped with HPLCs, GC and other testing instruments.

The Microbiological laboratory restricted to authorized personnel only. The laboratory activities, such as media, equipment preparation, testing, incubation and enumeration of microorganisms, and decontamination was segregated. There were appropriate entry and exit procedures, including gowning procedures.

The following tests performed by the laboratory: Microbial limit test, sterility test, bacterial endotoxin test, testing of different water samples and viable environmental monitoring. Media was prepared in-house as per SOP for Handling and Usage of Culture Media.

The following documents reviewed during the inspection:

- SOP for Bacterial Endotoxin Test
- Bacterial Endotoxin Test for Product Oxytocin Injection BP 10 IU/ml
- SOP for Sampling and Testing of Rubber Stoppers, Aluminium Seals/Vials/ Ampoules and Breathable Paper
- Bioburden Test Report for Rubber Stoppers/Aluminium Seals/Vials/Ampoules/Bio-Breathable Paper for Aseptic Media Fill Ampoule
- SOP for Operation and Calibration Procedure for Micropipette
- SOP for Handling and Usage of Culture Media
- Growth Promotion Testing Record for SCDM Media
- SOP for HPHV Steam Sterilizer Load Pattern
- Log-Book for HPHV Steam Sterilizer
- SOP for Handling and Usage Procedure for Bioball Microbial Cultures
- Format for Biological Indicator Study

The following Protocols and/or Summary Reports reviewed:

- Requalification Protocol for HPHV Steam Sterilizer Equipment
- Sterility Test Method Validation Protocol for Oxytocin Injection BP 10 IU/ml
- Summary Report for Bacterial Endotoxin Analytical Method Validation of Oxytocin Injection 10 IU/ml

Testing of starting materials and finished products

QC testing for starting materials and finished products conducted according to approved specification and test methods. SOP for Receipt, Sampling, Testing and Releasing of Raw Materials were reviewed. The sample receiving, and distribution register checked.

Computerized systems were used in the QC laboratory for starting material and product testing and data management. HPLCs and GCs networked by software in its QC laboratory. The company had personnel secured password-controlled procedure for log-in with staff level privileges. The computer access control, authorization of the functions was spot checked during the visit to QC laboratory. Computerised system validation and qualification not reviewed in detail due to time constraints.

Stability monitoring of FPPs

Stability studies managed according to an approved SOP. A range of stability chambers were available at the QC laboratory. The stability sample management of Oxytocin Injection products checked in QC laboratory. Stability study analytical report was spot checked.

Reserve/retention samples

SOP for Sampling, Storage, Inspection and Destruction of Control Sample for Finished Product was reviewed and discussed.

Part 3	Initial 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, ***Steril-Gene Life Sciences Pvt Ltd***, located at ***No. 45, Mangalam Main Road, Mangalam Village, Villianur commune, Puducherry, 605110, 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 2 years, provided that the outcome of any inspection conducted during this period is positive.

Part 4	List of GMP Guidelines referenced in the inspection report

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-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://www.who.int/docs/default-source/medicines/norms-and-standards/guidelines/production/trs1010-annex8-who-gmp-heating-ventilation-airconditioning.pdf?sfvrsn=c77698e2_0

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***
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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***
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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**
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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