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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	Sun Pharmaceutical Industries Limited (SPIL) - Paonta Sahib
Corporate address of manufacturer	Sun Pharmaceutical Industries Limited Sun House, CTS No.201 B/1, Western Express Highway, Goregaon E, Mumbai 400063, India
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Sun Pharmaceutical Industries Limited Village Ganguwala, Paonta Sahib, District Sirmour, Himachal Pradesh, 173 025 India
Unit / block / workshop number	A, C, D, E, F
Inspection details	
Dates of inspection	19-21 April 2023
Type of inspection	Routine GMP Inspection
Introduction	
Brief description of the manufacturing activities	SPIL Paonta Sahib is licensed by the Department of Health and Family Welfare, Himachal Pradesh to manufacture various formulations of tablets, hard and soft gelatin capsules. Tablets and hard gelatin capsules are manufactured in Blocks A, C, D, E, F and G. Block H is dedicated to oncology tablets and has a separate laboratory. Soft gelatin capsules are manufactured in Block B. The chemical and microbiological laboratories are in a separate building and accommodate the quality control needs of all manufacturing blocks except block H. The stability laboratory is housed in a separate building. No β-lactam antibiotics and no steroid products are manufactured on-site.
General information about the company and site	Sun Pharmaceutical Industries Ltd (SPIL) was established in 1983 and its headquarters are located in Mumbai. It is one of the world's largest specialty generic pharmaceutical companies with over 40 manufacturing sites across the globe. The site was established in 1995 and it is located near the town of Paonta Sahib, approximately 50Km from Dehradum. The site consists of 8

	manufacturing blocks and a facility manufacturing fermentation-based API.
History	The site was last inspected by WHO in October 2017. A desk assessment was carried out in October 2020. The site was inspected by Health Canada in June 2022. The site was periodically inspected by CDSCO.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Documents reviewed included but were not limited to: • Quality Manual – management review meetings • Organization Chart • Job descriptions for key personnel • Personnel training and hygiene • Product Quality Review • Quality Risk Management • Responsibilities of the quality unit and production • Complaints and Recalls • Deviation handling and CAPA • Change control • OOS and OOT investigations • Material release • Self-inspection and vendor qualification • Validation and qualification • Equipment calibration • Data integrity • Sampling and testing of materials • Batch processing records • Materials management system • Analytical methods – stability • HVAC system • PW system Areas visited: • Starting materials, packaging materials and FPP warehouses • Sampling and dispensing areas • Tablet and capsule manufacturing operations • QC laboratories
Restrictions	The inspection was restricted to manufacturing blocks relevant to the products approved by WHO PQ.
Out of scope	Manufacturing Blocks B, G, and H were not inspected since no WHO PQ products were manufactured in these blocks.
WHO products covered by the inspection	HA286 Lamivudine/Zidovudine Tablet, Film-coated 150mg/300mg HA698 Abacavir (sulfate)/Lamivudine 600mg/300mg Film-coated Tablet

	HA306 Efavirenz Tablet, Film-coated 600mg HA323 Lamivudine/Nevirapine/Zidovudine Tablet, Film-coated 150mg/200mg/300mg HA525 Lamivudine/Tenofovir disoproxil fumarate Tablet, Filmcoated 300mg/300mg HA708 Dolutegravir (Sodium) Tablet, Film-coated 50mg HA742 Atazanavir (sulfate)/Ritonavir Tablet, Film-coated (pending) CV015 Molnupiravir Capsules, hard 200mg(pending)
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
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 (where applicable)**

1. Pharmaceutical quality system

The Global Quality Manual described the framework and principles of the company's QMS. It outlined the Sun Pharma's commitment to follow GxP guidelines and it was aligned with ICH Q10 principles. A procedure was established for the preparation and lifecycle management of the Quality Manual. Periodic review of the QM and Policies took place every five years. QA and QC functions were independent of production function, and this was reflected in the organogram.

Management review meetings

Management review meetings were conducted both on global and on-site level. A procedure providing instructions on the organization of the corporate level quality review board meetings was available. On-site management review meetings were held monthly and were governed by a written procedure. According to the procedure, the Site Quality Head was assigned as the chairperson of the review meetings and the procedure defined the persons responsible for attending these meetings. Delegation of attendance was detailed in job descriptions. The 2023 annual schedule for management review meetings was presented. The minutes of the February and March 2023 meetings were provided.

QRM

Quality Risk Management principles were integrated in the site's QMS. A procedure was in place to detail the systematic approach for the identification, analysis, classification, communication, and overall management of risk. The following risk assessments were reviewed:

- HACCP Assessment of the Warehouse operations

- FMEA Assessment of the Warehouse operations
- Risk and Impact Assessment of Raw Material reduced testing on Finished Product – Tenofovir API

Product Quality Review

A product quality review SOP was in place. The review period was set to 12 months and a PQR rolling plan was established. The Schedule Log for APR 2022-2023 was reviewed. APQR had to be completed within two months after the end of the review period. In case less than 25 batches were manufactured in the review period, data from batches from previous reviews could be used for the statistical evaluation.

The following PQRs were reviewed:

- Lamivudine/Zidovudine 150/300mg tabs (1/2022-12/2022)
- Lamivudine/Zidovudine 150/300mg tabs (1/2021-12/2021)
- Emtricitabine/Tenofovir 200/300mg tabs (1/2022-12/2022)
- Emtricitabine/Tenofovir 200/300mg tabs (1/2021-12/2021)

Change control

A procedure for the management of changes was made available. The procedure covered change requests in GxP systems, products, processes, procedures, and documents that could impact product quality/compliance. The SOP was applicable only to the SPIL Paonta Sahib. The initiator of a change logged the Change Control Record (CCR) in Trackwise and the Department Head was responsible for reviewing the proposed change before being assessed by QA and the CCR Evaluators. QA was also responsible for verifying the implementation and evaluating the effectiveness and closure of a change.

The list of 2022 CCRs was provided. The following changes were reviewed:

- 25.01.2022 Installation of new camera system on blister packing line
- 23.02.2022 To facilitate review, approval and issuance of artworks & PO/PI of Dolutegravir/Lamivudine/Tenofovir DF TAB 50/300/300mg 180BTL - WHO market
- 01.07.2022 To revise Formulation and Manufacturing Instructions for Lamivudine and Tenofovir Disoproxil Fumarate tabs 300/300mg -WHO market

Deviations

The SOP for deviation management was made available. The deviations were reported, evaluated, investigated, managed, resolved, documented, and trended through the Trackwise system. The company defined “planned” and “unplanned” deviations. Examples of deviation handling were reviewed from the 2022 and 2023.

2. Good manufacturing practices for pharmaceutical products

Basic principles of good manufacturing practices were generally well defined in SOPs and implemented. Manufacturing processes were adequately described and documented in BMRs and BPRs. Records were made during manufacture. Qualifications, validations, calibrations, and maintenance were performed according to prepared protocols and plans. Required resources were available, including adequate premises, equipment, and utilities as well as qualified and trained personnel.

3. Sanitation and hygiene

Premises and equipment were generally maintained at an acceptable level of cleanliness, and they were appropriately labelled, and appropriate records were maintained. There was appropriate gowning in all areas for staff and visitors, including pictorials and hand washing and sanitization before entry to production areas.

4. Qualification and validation

Validation master plan

The validation master plan was presented. The policy as well as the validation and qualification strategies were clearly defined.

The periodic performance verification calendar for the Block A and year 2023 was presented.

Process validation

The process validation (lifecycle approach – process design stage to commercial production) procedure was also made available. This procedure was related to the validation of a new or an existing process and was applicable to all the processes at the site. The process performance qualification combined the qualified facility, utilities, equipment and trained personnel with the commercial manufacturing process, control procedures, and components to produce commercial batches.

The process performance qualification protocol of Molnupiravir capsules 200 mg (market: WHO) was approved on 07.01.2022. Three (3) exhibition batches had to be manufactured for WHO.

The process performance qualification report for the same product was approved on 18.01.2023. The 3 exhibition batches were manufactured in January 2022. All the parameters and quality attributes were compared between the 3 exhibition batches and the process development batches and were found similar. Proposals for parameters for future commercial batches were described in the report. Stability results after 9 months were presented and found within the specifications.

Empower 3 qualification

The following documents were reviewed in relation to the installation of the new Empower 3 server and software:

- Computerized Systems Validation Plan for Empower This document defined the overall approach to validation, implementation and roll-out the new Empower 3 software.
- Computerized Systems Validation Report for Empower 3
- Computerized Systems Test Report for Empower 3

Cleaning validation

The cleaning validation SOP was presented. QA was responsible for the preparation and approval of cleaning validation/verification protocol. The procedure adequately described the cleaning validation lifecycle which included 3 phases:

Phase 1- Cleaning process design and development

Phase 2- Cleaning process qualification

Phase 3 – Ongoing monitoring

The following documents were reviewed:

- Cleaning Validation Approach
- Product Matrix
- Annexure V: Identification of worst-case molecule for general product matrix
- Protocol for cleaning validation of manufacturing equipment
- Summary report for cleaning validation of manufacturing equipment
- Cleaning validation report of FBD

5. Complaints

The procedure for the management of product quality complaints (PQC) was reviewed. This was a site-specific SOP. The assessment of the criticality level (critical, major, or minor) used 3 criteria: severity, occurrence, and detectability. In case of a critical quality complaint, the authorities had to be informed. All the complaints had to be investigated to determine the possible root cause of the quality defect. Special attention was given to a quality complaint associated with counterfeiting. Further CAPA had to be initiated by the site PQC coordinator. A report was prepared, and after approval by QA, a response was sent to the complainant. A trend analysis was performed and included in the annual product quality review.

Some examples of complaint investigations were reviewed.

6. Product recalls

The SOP for the management of product recall was reviewed. The different stages of responsibility were clearly defined. The depth of the recall was also defined (consumer level, retail level, wholesaler/distributor level). A mock recall was scheduled, in order to challenge the recall process. A recall list for the year 2022 was presented.

7. Contract production, analysis and other activities

The documentation related to the asset transfer agreement between Ranbaxy Laboratories Limited and Sun Pharmaceuticals Limited, was reviewed.

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

Suppliers' qualification and follow-up

The SOP related to vendor management was presented. The qualification process of new vendors was reviewed. There was an audit team, which was centrally located at the headquarters of the company in Mumbai and was responsible for auditing and approving suppliers. Examples of supplier qualification and requalification were reviewed.

9. Personnel

In general, personnel interviewed had the necessary qualifications and practical experience. The site's organization chart was provided, and it was an Appendix of the SMF. The organization chart reflected the hierarchy in the Quality and Production units as well as their independence. Responsibilities and duties were defined in written job descriptions which were prepared according to a written procedure. Job descriptions were reviewed biannually, unless earlier required.

The following job descriptions were reviewed:

- Stability Manager
- Group Leader Quality Control – Raw materials
- Senior Manager Quality Control – Finished Product and Validation
- Quality Control Manager- Packaging Material
- Production manager block B,
- Production manager block D/E,
- Production manager block G/H
- Senior manager quality control
- Senior general manager quality
- Senior general manager operations

- DGM quality assurance.

Three shifts in production and two shifts in quality control were in place. Most personnel were permanent both in production and quality control. Some workers for handling receipt of materials were contracted and their training was spot-checked.

10. Training

The Learning Management System (LMS) system was not operational at the time of inspection and therefore spot checks on hard copies of training exercises were made. More specifically, the following training records were reviewed in relation to the installation of the new Empower 3 server and software:

- Empower Qualification training
- Performance Qualification of Empower on test cases
- Computerized System Test Management

11. Personal hygiene

Personal hygiene at the facility was guided by written procedures. The SOPs described the various hygiene practices aiming at protecting product quality. The hygiene practices included hand washing and gowning instructions, reporting of illness, exclusion of certain practices in production areas. In general personnel followed good hygiene practices.

12. Premises

Layouts of the facilities were made available. In general, premises were constructed, designed, and maintained to suit the operations to be carried out and prevent the risk of contamination of materials and products with some exceptions which were detailed in Part 3. Different operations were inspected during the tour of the manufacturing blocks A, C, D, E and F. These blocks were built in a modular way to accommodate an increase in manufacturing capacity over the years. Appropriate HVAC systems had been installed and core manufacturing areas were appropriately segregated. There were separate warehouses for raw materials and finished products. Sampling and dispensing facilities were located in the warehouse. The chemical and microbiological laboratories were housed in one building and accommodated the quality control needs of all manufacturing blocks except block H. The stability laboratory was located in a separate building.

13. Equipment

In general, equipment was installed and adequately maintained to meet the requirements for the dosage forms manufactured. Production equipment was of good standard and appeared to be well maintained. The workflow in the facility was appropriately designed, and the equipment appeared to be installed to facilitate production and reduce the risk of contamination and mix-ups. All production equipment reviewed was identified as to its content or cleanliness status by appropriate labels. Cleaning and equipment maintenance logbooks were established. Spot checks on daily verification of the scales in the sampling and dispensing areas were made. Similarly, the use and cleaning records of the sampling and dispensing booths were reviewed during the tour of the facilities.

14. Materials

There were procedures in place describing receipt, storage, and management of raw materials. Incoming materials were purchased from approved vendors, sampled, and tested according to

specifications and testing procedures. Upon receipt of raw and packaging materials, the materials were recorded in a logbook-register. SAP was used to manage materials, intermediates and finished product inventory and status.

The storage areas for quarantine and approved raw materials were visited. All materials were labelled with the appropriate labels based on their status, for example under quarantine, approved. SAP was used to generate these labels. Sampling of raw and packaging materials was performed in separate rooms.

15. Documentation

The SOP on document management (SOP on SOPs) was reviewed. The document described the workflow from the document creation, internal review, and final approval. Once the document was approved, the site coordinator was in charge to define the review period and the effective date of implementation. After the review of an expired document, if no modification/update was needed, the SOP would be assigned a new version and an extended validity period of 3 years.

The document was clear and comprehensive.

16. Good practices in production

The different production blocks were visited, and different operations were inspected on each manufacturing block. Areas inspected included the dispensing areas, granulation, compression rooms, coating rooms and primary and secondary packaging areas. BMRs and BPRs of batches being manufactured during the tour were spot checked as well as maintenance and calibration of equipment.

17. Good practices in quality control

The Quality control laboratories were separated from the production areas and tasked with the physical, chemical, instrumental and microbiological analysis of starting, packaging, and intermediate materials, as well as finished pharmaceutical products. The QC laboratoty was appropriately organized and equipped. Analytical equipment was installed in separate rooms and logbooks for use and maintenance of equipment were presented.

There was a procedure in place for monitoring PW. Every day at least one user point for total aerobic microbial count was sampled and tested. All user points were covered every 14 days. Samples were collected every day from the return loop for chemical and microbiological analysis. In addition, samples were collected every day, from the storage tank for chemical and microbiological testing. Finally, weekly tests for pathogens were conducted for every sampling point on the return loop and once every 14 days tests for pathogens were conducted on rotation of all user points. The following reports were reviewed:

- Monthly microbiological trend summary report for Manufacturing Block-D January 2023
- Monthly chemical trend summary report for Manufacturing Block-D

<u>OOS and OOT Results</u>

OOS and related CAPA were registered in Trackwise and followed the principles described in the relevant procedure. Examples of OOS were reviewed along with relevant CAPA.

Similarly, OOT results were registered in Trackwise and were handled according to a written procedure. Examples of OOT results were reviewed.

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, ***Sun Pharmaceutical Industries Limited (SPIL) - Paonta Sahib***, located at ***Village Ganguwala, Paonta Sahib, District Sirmour, Himachal Pradesh, 173 025, 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-eight 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. Fifties 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***

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