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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	**European Egyptian Pharmaceutical Industries (EEPI)**
Corporate address of manufacturer	25th Km, Alexandria-Cairo Desert Road, Amriya, Alexandria P.O. Box 111 El Mansheya, Egypt
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Same as above
Unit / block / workshop number	Oral Solid Dosage (OSD) – Tablets
Inspection details	
Dates of inspection	6-8 November 2022
Type of inspection	Follow up inspection
Introduction	
Brief description of the manufacturing activities	European Egyptian Pharmaceutical Industries (EEPI) was granted manufacturing authorization by EDA for manufacturing, packaging, and testing pharmaceutical products for human use of the following dosage forms: Solid dosage forms - Tablets "effervescent & non-effervescent" - Hard gelatin capsules - Powder "effervescent & non-effervescent" filled in sachets Liquid dosage forms - Internal use (syrup, suspension, drops) - External use (spray "nasal, topical", solution, lotion) - Soft Gelatin dosage Form As well as dental supplies (manufacturing of hydroxyl Apatite)
General information about the company and site	European Egyptian Pharmaceutical Industries (EEPI) is a pharmaceutical company located on the outskirts of Alexandria city, Egypt, and is a member of Pharco Corporate. The site was certified for ISO 9001:2015, ISO 17025:2017, ISO 14001:2015, ISO 45001:2018 & ISO 13485:2016 and was operating

	under an integrated quality management system. The company indicated that no high-potency or potentially hazardous substances such as hormones and beta-lactam products are manufactured on-site.
History	This was the fifth WHO PQ inspection. The manufacturing site was last inspected by WHO PQ in December 2021. The site was periodically inspected by the Egyptian Drug Authority. During the last year the site was also inspected by the National Agency for Medicines and Medical Devices of Romania and ANVISA, Brazil.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	The inspection focused on the production of Sofosbuvir film coated tablets and the implementation of the CAPA plan as a result of the previous WHO inspection. Documents reviewed include but are not limited: - Job descriptions for key personnel - Training - Product Quality Review - Management Review - Complaints and Recalls - Deviation control - Change Control - OOS and investigations - Validation/ Qualification/ Calibration - Sampling and testing of materials - Batch processing records - Materials Management System - HVAC System <u>Areas inspected</u> - OSD Production operations with a focus on Sofosbuvir film-coated tablets 400 mg production - Quality Control (chemical laboratories) - Warehouses (raw materials (quarantine/release), packaging materials, finished product, rejected products)
Restrictions	The inspection was restricted to the production, quality control and storage of Sofosbuvir film coated tablets 400 mg
Out of scope	Products and production areas outside of the inspection scope weren't included in the scope of this inspection
WHO products covered by the inspection	HP003 - Sofosbuvir film coated tablets 400 mg

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**

1. Pharmaceutical quality system

In general, a Pharmaceutical Quality System was established, documented and implemented, with written procedures covering essential quality elements being in place. Several procedures had been amended according to the CAPAs for the deficiencies made following the last WHO inspection. The procedures that were reviewed and discussed during the inspection were generally of an acceptable standard.
Production and quality control operations were independently managed and specified in written form. GMP requirements were essentially being met.

Product Quality Review (PQR)

PQRs were conducted based on the SOP "Annual Product Quality Reviews" (for batches produced between October and September every year). The Sofosbuvir tablets (Grateziano) 400mg PQR for the period 01.10.2021 to 30.09.2022 was reviewed. The company had discontinued the production of Grateziano 400mg tablets batch size 10.08kg.
CAPA related to PQR observations identified during the previous WHO inspection had been applied and observations were adequately addressed.

Product Release

Product release was managed according to the SOP "Final Release". Work instructions for final release were also in place. The Quality Assurance Manager was responsible for final release.

Deviations

The procedure on handling deviations was made available. The deviation logs for 2021 and 2022 were reviewed. Deviations were classified as critical, major, or minor depending on their impact on product quality and GMP. According to the SOP deviations had to be registered as soon as they were identified. A spreadsheet was used to register deviations. Access was restricted to authorized personnel. After a new entry or an amended entry was made, the register was printed and approved from the QA manager. CAPA related to the observations identified during the last WHO inspection had been addressed. The following deviations were reviewed:

- Stability results and shelf-life extension of the product not included in the relevant PQR.
- Additional impurity identified in Grateziano chromatogram but not included in CoA.
- Malfunction in warehouse material entry door of the main warehouse.
- Copy, paste delete functions allowed by the software of portable Bruker Bravo spectrophotometer.

Change Control (CC)

A procedure for managing changes was presented. The changes were classified into major and minor and registered in the Change Control Index. No major changes had been recorded since the last inspection.

The following Change Controls were reviewed:

- Changing the method of analysis and final impurity profile of the API Sofosbuvir NPP upon the change notification of PBIC (API Supplier).
- Upgrading of the BMS software system to insert alert/alarm for monitoring temperature, relative humidity and differential pressure.
- Improvement of performance parameters for the method of analysis of Sofosbuvir degradation products.
- Change in Sofosbuvir degradation products method of analysis for Grateziano 400mg fc tab.

Quality Risk Management

Quality Risk Management was incorporated in different procedures and was based on ICH Q9 principles. The following risk assessments were reviewed:

- QRM report for API manufacturing process change in Sofosbuvir powder NPP,
- Risk analysis on Sofosbuvir manufacturing process changes.

2. Good manufacturing practices for pharmaceutical products

Good manufacturing practices were generally implemented. Manufacturing processes were generally adequately defined. The manufacturing processes and procedures were documented in the BMRs and BPRs. Product and processes were monitored, and the results were checked as part of the approval process for batch release.

3. Sanitation and hygiene

Premises and equipment were maintained at a satisfactory level of cleanliness at the time of the inspection. Change rooms for general, primary, and secondary manufacturing zones were in place, allowing for staff gowning and shoe changes. Pictorials for gowning and hand sanitization before entry to the production areas were available in change rooms.

4. Qualification and validation

The site had in place procedures for performing qualification/validation of facilities, equipment, computer systems, and processes. The latest Validation Master Plan, Process validation plan and Calibration/Qualification program including all the equipment, instruments, areas, and utilities for 2022 were reviewed.

Cleaning validation

Cleaning validation was managed according to the SOP "Cleaning Validation General Procedure". The worst-case scenario was determined based on a matrix that assessed solubility of API, potency of the product (therapeutic dose), toxicity of the API, cleanability. Permitted Daily Exposure (PDE) determination was calculated by a contracted Toxicologist. The selection of the worst-case molecule for solid dosage forms and manufacturing line as well as the latest cleaning validation report were reviewed. The cleaning validation approach had been updated according to the observations identified during the last WHO inspection.

Equipment qualification

During the previous inspection it was observed that the software of Portable IR spectrophotometer Bruker Bravo EQRM69 (installed in sampling room), allowed for files to be copied, cut, pasted, and potentially deleted. The company had applied CAPA and requalified the software and hardware.

The qualification of NIR Bruker EQRM18 installed in the same area (sampling room) was checked.

5. Complaints

Complaints were handled according to a written procedure. Complaints were classified according to criticality. Investigations were conducted to identify the root cause and confirm the nature of complaint. Involved NRAs were notified in case of critical complaints. Periodic review of complaints was performed every six months. A report was made available and due to the small number of complaints it included review of complaints from January 2021 to June 2022. One complaint had been registered in 2022.

6. Product recalls

There was a procedure in place for effectively recalling defective products/batches from the market. The procedure provided appropriate instructions on the actions to be taken to withdraw a product/batch from the market to protect public health. Recalls were classified based on urgency and level of recall. The most recent mock recall was carried out in December 2021.

7. Contract production, analysis and other activities

Manufacturing and laboratory activities related to Sofosbuvir f.c. tablets were not outsourced.

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

Self-inspection

Internal audit was performed at least three times per year, one round for GMP, one for pharmacovigilance and one for QMS based on the SOP on Internal Audits. A list of auditors (last updated 15.02.2022) was in place.

The internal annual audit plan tracker for 2022 and the report of internal quality audit for warehouse (conducted 23-25.08.2022) were checked.

Suppliers' approval

The selection, evaluation, and approval of raw and packaging materials suppliers were performed according to SOP "Supplier Qualification and Evaluation Program".
Based on the risk assessment to the manufacturing process of the product and to the potential harm to the patient, materials were classified into six categories from high risk (API) to low risk. Suppliers of raw materials and packaging materials were assessed for their quality system through an evaluation questionnaire and by conducting an audit, when required. A risk priority number was established, and audit frequency was assigned based on this calculation. The suppliers could be characterized as approved, qualified, or certified. An annual evaluation was performed. An approved supplier list for raw materials, last updated on 24.09.2022 was available.
The following documentation regarding supplier qualification was reviewed:

- Pharco B International (2) for Chemicals (PBIC - Sofosbuvir API manufacturer): the evaluation questionnaire (01.10.2021), the final supplier annual evaluation report (28.12.2021) and the quality agreement between PBIC and EEPI (09.2021).
- Roquette, France (Pearlitol 200SD-Mannitol) the final supplier annual evaluation report (2021).
- HDPE Jars & Cap (packaging materials) final supplier annual evaluation report (2021)

9. Personnel

There were approximately 1130 staff working on-site, in three shifts, with appropriate qualifications, experience, and training. Job descriptions were established in accordance with a written procedure. The job description of the Quality Assurance Manager was reviewed. Qualification, competencies, and responsibilities were defined. Acceptance of responsibilities was documented. Delegation of duties was also made available.
An organizational chart presenting the hierarchy in the different departments was available.

10. Training

Training was conducted according to a training plan which was quarterly updated. Records for completion of training sessions and attendance were maintained.

11. Personal hygiene

A gowning procedure to enter the warehouse and production facilities was in place. A hand washing facility, mirrors and depicted gowning procedures were provided in the change rooms. In general, the gowning procedure was found adequate.

12. Premises

Generally, premises were located, designed, constructed, and maintained to suit the operations being carried out. The production area was laid out to allow production to occur in areas connected in a logical order, corresponding to the operations sequence and the required cleanliness levels. Solid and liquid dosage forms were manufactured in different areas of the same building. There were separate warehouses for storage of raw and packaging materials and finished products. Receiving and dispatch bays were separated and protected materials and products from weather conditions.

The QC laboratory was well designed and equipped with adequate space for the various activities.

13. Equipment

In general, equipment was installed in a rational manner to accommodate manufacturing processes. It was maintained in a good state of repair and each piece of equipment was assigned a unique identification number. Calibration and qualification labels were placed on each equipment. Equipment for Sofosbuvir production was not dedicated. Equipment used in tablet manufacturing and packaging were the following:

- Powder Sieving Machine
- Powder milling & sieving machine
- Tablet Compression machine connected with in-line tablet examination unit for weight/thickness/hardness- tablet dedusting-metal detector
- Tablet Coating machine
- Tablet counting and labelling machine.

14. Materials

Incoming raw materials/packaging materials were unloaded in the receiving bay. Materials received were checked against the delivery note. A check list (W/75-8002/6/C) was used to verify and document the origin, integrity, quantity, and storage conditions during transport. The receipt checklists for Clindamycin Phosphate Batches P-211016C and P211103C, Sucrose Batches 022300936 and 022100935, Saflower oil Batch 12060/100927 and Amlodipine API were checked.

Materials were quarantined after receipt, sampled, tested, and released for use in production.

Returns

Handling of returns was handled in accordance with a written procedure The procedure described how products/batches were returned back to the warehouse, registered in the ORACLE system, quarantined and the decision-making process for reworking, release or destruction.

15. Documentation

In general, documents were designed, prepared, reviewed, and distributed according to a documented procedure. Quality system documents were regularly reviewed and kept up to date. Approved specifications and testing procedures were available for raw materials, packaging materials and Sofosbuvir finished product. Batch manufacturing records (BMRs) were retained for each batch processed.

16. Good practices in production

All production areas for Sofosbuvir 400mg film-coated tablet were visited. The product was produced in shared OSD facilities. Areas inspected included the receiving area for raw materials/packaging materials, the warehouse for raw materials, the sampling suite for sampling raw materials and a separate room for sampling packaging materials, the dispensing area equipped with two dispensing booths and balances, the granulation area, the milling and blending rooms, the compression room, the coating area, primary and secondary packaging rooms, the IPC room, the washing room and the spare equipment and tools room. A BMS was controlling all the operations of the HVAC system.

During the tour, the following documentation was checked:

- The Logbook data recording among the others the sieving integrity check.
- The SOP for sampling of raw materials
- The Work Instructions describing the sampling steps for raw materials
- The logbook for raw materials sampling
- The logbook of Portable IR spectrophotometer Bruker Bravo
- The logbook for clearance of the sampling room for raw materials
- The logbook for daily adjustment of the sampling balances
- The SOP for sampling of packaging materials.
- The logbook for use of the dispensing booth
- The logbook of the dry milling machine
- The SOP for IPC of solid dosage forms
- The Batch production record of the product Neurovit tab Batch 3033568 (granulation).
- The Batch production record of the product Neurovit tab Batch 3033553, (compression).
- The Batch production record of the product Neurovit tab Batch 3033566, (coating)
- The Batch packaging record of PerLoc tab Batch 3041010, (primary packaging)

Reprocessing and reworking were carried out following the principles described in a written procedure. QA was responsible for deciding if a batch could be reprocessed. R&D was responsible for initiating a risk assessment and determining the reprocessing or reworking steps, additional testing, and stability studies to be applied. Reworked and reprocessed batches were issued the same batch number with the addition of the letter (R) and batch records had to be completed for the reprocessing that was carried out.

17. Good practices in quality control

Quality Control (QC) operations were independent of production. The QC was designed and equipped with physicochemical, stability studies and microbiological testing facilities. The analytical laboratory for testing raw materials and the analytical laboratory for testing finished products were visited. The reconciliation of samples logbook was reviewed.

Testing of raw materials, Purified Water and finished products

Records of the following raw materials and finished products testing as well as purified water were reviewed:

- Certificate of analysis and analytical records for Pyridoxine Hydrochloride Batch No. PH18113040
- Certificate of analysis and analytical records for Grateziano 400mg fc tab Batch No. 3104001
- The protocol and report for water system monitoring

Primary/Working standards

Primary/Working standards were appropriately maintained and stored. The following documentation was reviewed with regards to standards:

- The logbook for registering the consumption of reference standards in raw materials analytical laboratory.
- The SOP for handling and storage of primary standards
- The SOP for qualification, handling and storage of working standards
- The logbook for registering the consumption of in finished product analytical lab.
- The standardization reports of Sofosbuvir Working Standard

- The logbook for registering the consumption of reference standards in the finished product analytical laboratory.

Analytical method

The following analytical methods were reviewed:

- Grateziano 400mg fc tab method of analysis.
- Grateziano 400mg fc tab method of analysis for Sofosbuvir degradation products.
- Grateziano 400mg fc tab content uniformity.
- Grateziano 400mg fc tab identification method of Sofosbuvir.

Out of specification results

The SOP for "Evaluation and Investigation of Out of Specification (OOS) Test Results" was discussed. The SOP described the investigation process. A limited number of OOS results was recorded in the logbooks, with the majority of them attributed to error in dilution during sample preparation.

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, ***European Egyptian Pharmaceutical Industries (EEPI)***, *located at* ***25th Km, Alexandria-Cairo Desert Road, Amriya, Alexandria, P.O. Box 111 El Mansheya, Egypt*** 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 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