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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	**PT Tunggal Idaman Abdi (hereafter TIA)**
Corporate address of the manufacturer	P O Box 4009, JI. Jend. Ahmad Yani no. 7 Jakarta, 13230 Indonesia
Inspected site	
Name & address of inspected manufacturing site if different from that given above	PT Tunggal Idaman Abdi P O Box 4009, JI. Jend. Ahmad Yani no. 7 Jakarta, 13230 Indonesia Latitude: 6.205071 South Longitude: 106.874006 East
Unit/block / workshop number	Plant-2 (hormone injectables)
Inspection details	
Dates of inspection	7-11 August 2023
Type of inspection	Routine GMP inspection
Introduction	
Brief description of the manufacturing activities	PT Tunggal Idaman Abdi (TIA) was located at Jalan Jend. Ahmad Yani No.7, Jakarta 13230, Indonesia, and the manufacturing site was comprised of the following main buildings: - Non-Hormone Plant-1-area: 2213 m^2 - Hormone Plant-2-area: 3032 m^2 - Main Warehouse area (2 floors): 984 m^2 - QC Laboratory: 184 m^2 - Workshop - Engineering area: 843 m^2 <u>Plant-2</u> manufactures hormone products, and the injectable section was under the scope of this inspection. It was comprised of the following floors: - Floor 4: 1,001 m² (Utilities for tablets line) - Floor 3: 1,537 m² (Production line: tablets + spare room for expansion) - Floor 2: 1,537 m² (Utilities for injectables line) - Floor 1: 1,537 m² (Production line: injectables) An additional warehouse for the storage of finished goods and packaging

	material was located at Jl. Jend. Ahmad Yani No.2 Jakarta 13210, about 5 km from the factory.
General information about the company and site	PT Tunggal Idaman Abdi (TIA) was established in 1970 and has a manufacturing facility located at Jalan Jend. Ahmad Yani No.7, Jakarta 13230, Indonesia. The Hormone Production Plant 2, consisting of 4 (four) floors of the building with a total area of 1500 m^2 was constructed in January 2012 for hormone production capacity for both injection and oral reproductive health products. Plant 1 (Non-Hormone) and Plant 2 (Hormone) are physically separated.
History	The manufacturing site has been routinely inspected by the WHO Prequalification Inspection Services for *Medroxyprogesterone acetate* (MPA) injection. The last on-site inspection of the TIA was performed in May 2018. In addition, the manufacturing site has been routinely inspected by the National Agency for Drug and Food Control (NADFC), and the most recent inspection was performed in August 2022.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	The reviewed documents included but were not limited to: - Pharmaceutical quality system - Training - Complaints - Process validation - Qualification and requalification - Equipment calibration Sites visited: - Filling lines 1 & 2 - QC laboratories, including chemical and microbiological - Water for injection - Pure steam generator (PSG)
Restrictions	The inspection was restricted to the production of the Medroxyprogesterone acetate (MPA) suspension for injection, 150 mg/ml.
Out of scope	All other products and production facilities on the site were outside the inspection scope and were not visited.
WHO products covered by the inspection	RH090 Medroxyprogesterone acetate Suspension for injection 150mg/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	Nonconformity
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
RO	Reverse osmosis
SIP	Sterilization in place
SMF	Site master file
SOP	Standard operating procedure

URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer
WFI	Water for injection

Part 2	**Summary of the findings and comments (where applicable)**

1. Pharmaceutical quality system

A documented system for quality assurance was established, with procedures covering key quality elements in place. The quality department was divided into QA and QC and was separate from the production department. Operations were defined and documented, and critical GMP requirements were essentially met. The procedures reviewed and discussed during the inspection were generally acceptable.

The PQR procedure was reviewed, and it was noted that the PQR was performed based on the number of batches manufactured/dispositions. The scope of the PQR included raw materials, packaging materials, in-process data, product process capability, finished product analysis data, deviations, OOS, changes, stability, CAPA, and other areas. Minitab was used to calculate the process capability. A minimum of 30 batches were required to calculate process capability.

The quality risk management (QRM) procedure was discussed and noted that the FMEA tool was used to perform the risk assessment. In addition to the QRM procedure, a separate procedure, "Basic tools of quality management," was available, which applies to troubleshooting and investigation purposes such as the Ishikawa diagram, FMEA, 5 Whys, simple statistical process control, Pareto chart, process flow diagram, input-process-output (IPO) diagram, affinity diagram, run chart, and check sheets. A logbook in the form of a spreadsheet was maintained.

Change control procedure stipulated the handling and impact of change controls, which applied to new changes, including changes related to the production process, equipment, utilities, facilities, materials, and systems. The procedure described the changes that do not require change control initiation (e.g., change of working hours), including changes that should be notified to the national regulatory authority and WHO PQ. The changes were classified as major and minor. Change control related to the introduction of Line 1 was briefly reviewed as part of the PQR.

The management review procedure guided how to perform the MR to improve quality systems and processes. It was performed at two levels: by the Head of the Manufacturing Plant and the Top management (Board of Directors and Managing Director). The procedure described the contents of the MR meeting, and the minutes of the meetings were recorded. The corrective actions were implemented as per the CAPA plan.

The SOP for batch disposition guided the disposition of raw materials, packaging materials, bulk/intermediates, and finished products. The QA manager was responsible for batch release. She authorized the QA supervisor to release the finished product batches in her absence. A checklist was used to verify aspects of the process, packaging, test report from QC, and QA evaluation. The batch analysis certificate was prepared after the batch was disposed of. The incoming materials were released by the QC manager, and in her absence, she delegated this responsibility to the QC supervisor.

The deficiencies related to this section have been adequately addressed and will be verified during future PQ inspections.

2. Good manufacturing practices for pharmaceutical products

Good manufacturing practices were generally implemented. Necessary human and physical resources, including adequate premises, equipment, and utilities, were provided for the current operational level of MPA injection manufacturing activities. The manufacturing processes followed procedures as defined and documented in the BMRs. The personnel were appropriately qualified.

TIA is a multiproduct facility, and two products (containing MPA and a combination of MPA and Estradiol Cypionate injection) were produced on Lines 1 and 2. TIA confirmed that all parts that contact the product were dedicated to each product type, such as the hose/silicone tubing, nozzle, needles, compounding tank, holding tank, etc.

The deficiencies related to this section have been adequately addressed and will be verified during future PQ inspections.

3. Sanitation and hygiene

Disinfection of clean areas was performed frequently following the SOP. More than one type of disinfecting agent was used. The disinfectants were sterilized before being used in Grade A and B areas. The hygiene facilities on the site appeared acceptable.

4. Qualification and validation

Validations and qualifications were performed according to the site policy and documented procedures. Necessary resources in production were provided, including qualified and trained personnel, adequate premises, equipment and services, appropriate materials, approved procedures and instructions, laboratories, and equipment for in-process and other controls.

The process validation protocol of Triclofem injection was reviewed. The process validation in 2022 was triggered by introducing a new mixing sterile vehicle tank, mixing tank, and holding tank, which was common for both Lines 1 and 2. Three batches were taken for the process validation using a batch size of 116L covering vehicle mixing, vehicle solution filtration, sterile API introduction, and mixing, filling, stoppering, and capping, followed by optical control (visual inspection) of filled vials. The process flow diagram was part of the protocol, which described step-by-step instructions, including in-process and QC testing. The compounding was divided into three steps, whereas filling was described under step 4. The sampling and analytical plan was part of the protocol.

Cleaning validation on filling Line-2 was performed in September 2018, whereas in September 2022, it was done on filling Line-1. The details of the cleaning validation for Line-1 were reported. The results for visual inspection, pH, conductivity, TOC, microbiological test, and endotoxin test were within specification.

The performance qualification of media-fill in the hormone injection plant was discussed. The scope of the media fill covered dispensing (Grade C) of materials, vehicle mixing (Grade C), filtration method (0.22um), mixing bulk, transfer to holding tank, filling, stoppering, and crimping. Before filtration, the sample was taken for bioburden. After filtration, the sample was taken for sterility and growth promotion test (GPT) and was part of the media fill study. The acceptance criteria were provided in the procedure for initial media fill (3 runs with minimum units of media fill as per the batch size), including contamination limit and action. Similarly, periodic media fill criteria were described, requiring at least two runs per year. A list of media fill personnel qualifications for Line 2 was available (158) who had participated in media fill between March 2022 and March 2023. Two operators working in Line 2 were verified as participants in the media fill. A list of media fill personnel qualifications dated 28/04/2023 for Line-1 (153 personnel) who had participated in media fill between September 2022 and January 2023 were available. Two of the operators working in Line-1 were verified and found to be participating in the media fill.

The deficiencies related to this section have been adequately addressed and will be verified during future PQ inspections.

5. Complaints

The product complaint procedure was reviewed, and it noted that complaints were described as related to quality (physical, chemical, or biological damage to the product or packaging), adverse effects, or undesirable effects such as allergy, therapeutic or pharmacological effects such as non-efficacious and counterfeit. The complaints were received from the marketing and recorded in the logbook. A complaint form was used to record the complaints' details before the investigation. Based on the type of complaint, the investigation included a review of samples, physical, chemical, and microbiological tests, batch manufacturing records, and analytical records. For the local complaints, samples were mostly received, whereas, for the complaints from export markets, most of the time, samples were not received. The investigation was performed using quality management tools (SOP). Based on the criticality of the complaints, they were classified as minor, major, and critical. As a follow-up, CAPA includes recall of the affected product/batch if classified as critical. The timeframe for handling/closing complaints was described in the procedure.

The deficiencies related to this section have been adequately addressed and will be verified during future PQ inspections.

6. Product recalls

The procedure recall procedure was available. From the review of the PQR of MPA injection, it was noted that no recall was reported.

7. Contract production, analysis, and other activities

The company does not use a third party for the production/packaging of MPA injection. External laboratories performed some of the tests for MPA and excipients.

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

A self-inspection plan and SOP were in place.

TIA uses sterile MPA from a prequalified source, Farmabios S. p. A, Italy. The API manufacturer, Farmabios, was audited by the FPP manufacturer in Italy in July 2022, and the audit report was available. A third-party facility carried out the gamma radiation.

9. Personnel

There was an 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 was available. Key personnel responsibilities were required to be defined in job descriptions.

10. Training

Training was required to be conducted on an initial and ongoing basis. Re-training was required in the event of personnel errors resulting in a CAPA event. QA was responsible for training. The training program was not reviewed in detail in this inspection. Training effectiveness was evaluated during the inspection, e.g., filling machine set-up, visual inspection of vials, sterility testing, etc.

The deficiencies related to this section have been adequately addressed and will be verified during future PQ inspections.

11. Personal hygiene

Changing and washing before entry to production areas followed written procedures. In general, direct contact between the operator's hands and the starting materials and primary packaging materials was avoided. The protective clothing washing and sterilization operations followed standard operating procedures.

The deficiencies related to this section have been adequately addressed and will be verified during future PQ inspections.

12. Premises

In general, exposed surfaces of production areas were generally smooth, impervious, and unbroken to minimize the shedding or accumulation of particles or microorganisms. Production personnel performed environmental monitoring of the production areas. TIA informed that a change control was raised to change this practice and make QA responsible for the environmental monitoring program.

The clean rooms for MPA were surrounded by a Grade D corridor that gave good visibility to filling lines, Lines 1 and 2. In filling, the frontal view was good but no view of the rear side of the machine.

Also, there was no external visibility of some critical aseptic operations such as dispensing, compounding, autoclaving, filtration, and other areas.

Changing rooms were designed as airlocks and used to provide physical separation of the different stages of changing. Changing rooms were flushed with filtered air. The final stage of the changing room was the same grade as the area into which it leads. Changing rooms were equipped with crossover benches and mirrors.

QC laboratories for microbiological and chemical testing were separated from production areas. Entering QC was access-controlled.

The deficiencies related to this section have been adequately addressed and will be verified during future PQ inspections.

13. Equipment

The equipment installed in Lines 1 and 2 were used for manufacturing MPA injection and a combination product (MPA+ Estradiol Cypionate). All parts (such as hose, silicone tubing, nozzle, needles, compounding tank and holding tank) that come in contact with these two products were dedicated. Labels attached to the equipment clearly indicate equipment identification numbers, clean status, qualification status and due date. Equipment maintenance and cleaning were performed according to written procedures.

The deficiencies related to this section have been adequately addressed and will be verified during future PQ inspections.

14. Materials

Incoming materials and finished products were quarantined after receipt until they were released for use or distribution. Starting materials and packaging materials in the scope were purchased from approved suppliers. Materials and products were stored under the specified conditions.

This section was not inspected in detail due to time constraints.

15. Documentation

The documentation system was paper-based and was controlled by the QA department. Documentation was generally designed, prepared, reviewed, and distributed according to a documented procedure. Approved, signed, and dated testing procedures and specifications were available for starting and packaging materials and for finished products.

The deficiencies related to this section have been adequately addressed and will be verified during future PQ inspections.

16. Good practices in production

In general, the manufacturing process was well-designed and executed. The company performs manual visual inspection. From a quick glance at the visual inspection, the operators were following consistent inspection practices using a white/black background and looking for defects including cracks, black particles, mould issues etc. Reprocessing and reworking were not allowed for sterile products, whereas relabeling was carried out as and when required.
The manufacturing site undertook significant renovation work for the filling area. The deficiencies related to this section have been adequately addressed and will be verified during future PQ inspections.

17. Good practices in quality control

The QC Manager headed the laboratory. A total of 40 employees worked in the laboratory, including the heads of different sections. Two analysts were responsible for sampling raw materials and packaging materials, one for water sampling, nine employees for microbiology testing, and the rest for testing materials and finished products. The finished products were sampled by the production personnel and sent to the laboratory.

The QC personnel sampled the incoming materials and logged them into a logbook before assigning them to the analysts for testing. The laboratory was required to improve its current practices of assigning unique numbers to the incoming samples and products and ensure that all incoming samples, including stability samples, were adequately identified, labeled, and tested on time. The microbiology laboratory was relatively small in size for the number of activities being carried out. The incoming samples were recorded in logbooks (non-sterile samples were used for bioburden, whereas sterile samples were used for sterility testing). The sterility testing was performed under the Class 2B biosafety cabinet with a background of Grade B. The dehydrated media and prepared media were stored in a different room outside the main laboratory. Similarly, a separate room was provided for incubators.

The deficiencies related to this section have been adequately addressed and will be verified during future PQ inspections.

Part 3	**Conclusion – Inspection outcome**

Based on the areas inspected, the people met, the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, ***PT Tunggal Idaman Abdi*****,** located at ***PO Box 4009, JI. Jend. Ahmad Yani no. 7, Jakarta, 13230, Indonesia***,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. 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

7. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3.
Short name: WHO TRS No. 957, Annex 3
https://digicollections.net/medicinedocs/documents/s22358en/s22358en.pdf

8. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Sixth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 2.
Short name: WHO TRS No. 1044, Annex 2

TRS 1044 - Annex 2: WHO good manufacturing practices for sterile pharmaceutical products

9. WHO guidelines on technology transfer in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Sixth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 1044), Annex 4.
Short name: WHO TRS No. 1044, Annex 4
TRS 1044 - Annex 4: WHO guidelines on technology transfer in pharmaceutical manufacturing

10. 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

11. 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

12. 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

13. 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/

14. 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/

15. 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

16. 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

17. 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

18. 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)

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

20. 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)

21. 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

22. 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

23. 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

24. 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)

25. 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)

26. 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

27. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4. ***Short name: WHO TRS No. 1025, Annex 4*** https://www.who.int/publications-detail/978-92-4-000182-4