

**Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Active Pharmaceutical Ingredient Manufacturer**

Part 1		General information
Manufacturers details		
Name of manufacturer	Macleods Pharmaceuticals Limited	
Corporate address of manufacturer	Atlanta Arcade, Church Road, Andheri – Kurla Road Andheri (E), Mumbai 400059, India	
Inspected site		
Name & address of inspected manufacturing site if different from that given above	Macleods Pharmaceuticals Limited Unit V Plot No. 2209, CIDC, Sarigam, Dist. Valsad, State Gujarat, India 396155 GPS Coordinates 20°18.436'N, 72°50.987'E	
Synthetic unit /Block/ Workshop	Unit V Manufacturing Blocks A, B, C, D, E, F, G	
Inspection details		
Dates of inspection	23-24 & 26 June 2023	
Type of inspection	Routine GMP inspection	
Introduction		
Brief description of the manufacturing activities	The site consists of 8 manufacturing blocks (A-G, H is an independent block with separate and dedicated SMF) which are not product dedicated, and supportive buildings (e.g., engineering and utilities, electrical supply, tank farms, stores, laboratories etc.) Unit V manufactures APIs intended for medicinal products for human use. Highly sensitizing materials like beta-lactams are not manufactured on-site.	
General information about the company and site	Macleods Pharmaceuticals Limited (Macleods) manufactures and markets a wide range of pharmaceutical formulations and APIs. Its headquarters are in Andheri, Mumbai. Macleods has ten facilities: <ul style="list-style-type: none"> - Pharmaceutical Formulation (Unit I), Palghar (Maharashtra). - Pharmaceutical Formulation (Unit II), Daman (Union Territory). - Pharmaceutical Formulation (Unit III), Daman (Union Territory). - Research & Development (R&D) Centre, Andheri (Mumbai). 	

	<ul style="list-style-type: none"> - Active Pharmaceutical Ingredient and Pharmaceutical Formulation (Unit V), Sarigam (Gujarat). - Pharmaceutical Formulation (Unit VI), Nalagarh (Himachal Pradesh). - Pharmaceutical Formulation (Unit VII), Daman (Union Territory). - Pharmaceutical Formulation (Unit IX), Sikkim - Active Pharmaceutical Ingredient (Unit X), Dahej -Bharuch (Gujarat) - Pharmaceutical Formulation (Unit XI) Indore SEZ (MP). <p>Unit V is located at Sarigam GIDC Industrial Area, approximately 180Km north of Mumbai. The site is surrounded by open land and chemical industries.</p>
History	The last WHO on-site inspection was carried out in August 2016. A desk assessment was performed in 2020. The site has also been inspected by EDQM, MHRA, and US FDA
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	<ul style="list-style-type: none"> • Quality management • Personnel • Buildings and facilities (production blocks, laboratories, stores) • Process equipment • Documentation and records • Materials management • Production and in-process controls • Packaging and identification labelling of APIs and intermediates • Storage and distribution • Laboratory controls • Validation • Change control • Rejection and reuse of materials • Complaints and recalls • Contract manufacturers (including laboratories)
Restrictions	N/A
Out of scope	APIs not submitted to WHO Prequalification were out of the scope of this inspection. Block H was not included in the scope of this inspection.
WHO APIs covered by the inspection	Ethionamide Tenofovir Disoproxil Fumarate Emtricitabine Cycloserine Terizidone Oseltamivir Phosphate PAS (Aminosalicylate Sodium)

	Levofloxacin Hemihydrate Atazanavir Sulfate Pyrazinamide Linezolid Clofazimine Lumefantrine Dolutegravir Sodium Sulfadoxine Pyrimethamine Artemether Rifapentine Praziquantel Flucytosine Bedaquiline Fumarate Pretomanid Miltefosine Moxifloxacin Hydrochloride
Abbreviations	Meaning
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
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
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
KF	Karl Fisher
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology

MBL	Microbiology laboratory
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
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer

Part 2	Summary of the findings and comments
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1. Quality management

In general, a Pharmaceutical Quality System (PQS) was established, documented and implemented, with written procedures covering essential quality elements being in place. The Quality Manual provided the principles upon which the PQS was built. Senior management responsibilities were adequately defined. 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. There was a procedure in place for product release. The minutes of the most recent Management Review meeting were reviewed.

Quality Risk Management (QRM)

QRM was incorporated in the PQS and several procedures were in place describing its application in GMP processes, systems and operations. In general, appropriate instructions were included in the relevant SOPs for the identification, assessment, control, communication, review and mitigation of risks. The following documents were reviewed:

- Assessment report for Nitrosamine impurities in Clofazimine Drug Substance
- Assessment report for Nitrosamine impurities in Tenofovir Disoproxil Fumarate Drug Substance

Product Quality Review (PQR)

The company had established a procedure for conducting PQRs. These reviews were conducted annually, on a rolling basis, according to a written plan. The PQR had to be completed within 60 days from the target date. The Quality Assurance Department was responsible for conducting PQRs. The report would be reviewed by the manufacturing, warehouse, engineering, QC, and Regulatory Affairs departments. Statistical analysis was performed on critical process parameters and product quality attributes if 30 or more batches were manufactured during the review period.

The following PQRs were reviewed:

- Aminosalicylate Sodium (PAS) (Jan.-Dec. 2022), no batches were manufactured during the review period
- Dolutegravir Sodium (Jan.-Dec. 2022), 47 batches were manufactured during the review period
- Moxifloxacin Hydrochloride Monohydrate (Apr. 2022 – Mar.2023) 1 batch was manufactured during the review period
- Pyrazinamide (Jan. 2022 to Dec. 2022) 2 batches were manufactured during the review period

Deviations

A procedure for reporting, investigating, and resolving non-compliances, failures, events, and deviations in a timely manner, was in place. These unwanted and unforeseen incidents were recorded and monitored in TrackWise. An initial risk assessment was performed according to the categorization of the event (minor, major, or critical). The QA coordinator was responsible for evaluating the completeness and correctness of the incident report and assigning a Lead investigator to perform a root cause analysis. Investigations had to be completed within the given timelines, and appropriate CAPA had to be applied. Events were trended quarterly and annually. The trend analysis for the 1st Quarter 2023 was reviewed as well as the report for events occurred in 2022. CAPA were applied according to instructions detailed in a written procedure.

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

2. Personnel

There was a sufficient number of personnel who were suitably qualified through education, experience and training. Working roles and responsibilities were well defined in job descriptions. The company's reporting and administrative hierarchy was depicted in organization charts.

Personnel were required to wear protective clothing suitable for the type and stage of manufacturing. Appropriate change room facilities were provided. Smoking and eating were not permitted in manufacturing areas.

Induction and continuous training were conducted according to a written procedure. The effectiveness of training was evaluated using a n established template. Training course schedule and topics were available and examples of induction training were reviewed.

Any observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

3. Buildings and facilities

There were separate stores for raw and packaging materials, solvents, and intermediate/finished products. The temperature was monitored. Production operations were conducted in several buildings, divided into

the chemical processing area (reactor's area) and the finishing production area (clean area). A table highlighting the manufacturing steps and buildings/modules for each intermediate and API was made available.

Any observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

4. Process equipment

Equipment used in the manufacture of APIs appeared to be of appropriate design and size for their intended use. Equipment were not product dedicated. They were logically installed to suit manufacturing activities and processes. Appropriate cleaning, preventive maintenance, and calibration/qualification were performed as indicated in the relevant logbooks. As a general rule, there were two types of cleaning performed: batch to batch cleaning and to product change-over cleaning. The latter one was also applied after 10 consecutive batches of the same product were manufactured. Manufacture and material transfer took place in closed systems wherever possible. Examples of procedures and records for use and maintenance were reviewed:

- Hosepipe issuance and destruction record
- Procedure for the ID preservation and destruction of vibro-sifter, sieve/multi-mill mesh
- Operating and usage of sieve/mesh integrity checker

Any observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

5. Documentation and records

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, intermediates, and APIs. Batch manufacturing records (BMRs) were retained for each batch produced.

Any observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

6. Materials management The inspectors visited the material receipt area of the Block G warehouse. Receipt of raw materials was performed in accordance with a written procedure. A material receipt checklist was used. A list of approved vendors was available. The GRN was completed electronically in the ERP system and used for the management of materials. A quarantine area in the warehouse was available. It was noted that flammable solid materials (e.g., Potassium tertiary-butoxide) were quarantined in the same area as any other quarantined starting materials. The procedure for handling of retest materials was reviewed. There was a dedicated area for rejected materials.

There were three sampling rooms in Block G. One room in the production area served both as a sampling and dispensing room for hazardous materials. The other two sampling rooms were found in the warehouse. One of these two sampling rooms was dedicated to coloured materials. The procedure for the operation and cleaning of the sampling and dispensing rooms and the procedure for sampling, testing, release, and rejection of raw materials, as well as the relevant logbooks and examples of sampling records were reviewed. Each container of any key starting material or intermediate was sampled. For the rest of the materials, the rule of $\sqrt{n+1}$ was applied.

Qualification of Suppliers

Suppliers were qualified according to a written SOP. The purchase department was responsible for identifying new vendors. Three samples for analysis were requested for key starting materials or intermediates. The potential supplier had to complete a vendor questionnaire, which would be evaluated by the Corporate QA. Only suppliers of intermediates were audited. An annual evaluation of supplier performance was conducted and documented. Criteria for qualification and rejection of suppliers were established. Examples of supplier qualifications were reviewed.

Any observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

7. Production and in-process controls On the 1st day, during the site tour, the inspectors followed the production process of Tenofovir Disoproxil Fumarate in Block G. The manufacturing process flow chart was presented. Block G consisted of 4 floors (ground floor: warehouse, 1st floor: clean rooms, 2nd floor: purification/filtration, 3rd floor: reactions). Spot checks on the Tenofovir BMR were performed.

The second day the inspectors visited Block E where Clofazimine Stage I and Cycloserine Stage I were manufactured. The manufacturing process flow chart for Clofazimine and Cycloserine Stage I were made available. Block E consisted of 3 floors (ground floor: filtration, 1st and 2nd floors: reactions). Staging areas for solid materials were visited. Equipment usage and maintenance records were spot-checked.

On the same day, inspectors visited Block D where Cycloserine Pharma was manufactured. Block E consisted of 3 floors (ground floor: clean rooms, 1st floor: extraction/filtration, 2nd floor: reactions). The Cycloserine Pharma manufacturing process flow chart was presented. Cycloserine Pharma BMRs were spot-checked during the tour. Clean rooms where centrifugation, drying, milling, and packing were performed were visited. Equipment records for use, cleaning, and maintenance were reviewed.

Any observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

8. Packaging and identification labelling of APIs and intermediates

The procedure for issuing labels after packing was reviewed. The labelling process for Cycloserine Pharma was spot-checked. After packing, production personnel issued two labels, one to be placed between the two LDPE bags and one to be affixed on the external side of the container. Safety seals were placed on each container by production personnel in the presence of QA personnel. Records and inventory of safety seals were maintained. Finished products were placed in quarantine with appropriate labels. QA personnel was responsible for affixing release labels on API containers.

Any observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

9. Storage and distribution

Finished APIs were stored in a designated warehouse and held in quarantine until released by the authorized person. The ERP system was used to control status, stock and distribution. APIs and intermediates were released for distribution after they had been released by the Quality Unit.

10. Laboratory controls

Quality Control (QC) operations were independent of production. The QC was designed and equipped with chemical, instrumental, and microbiological testing facilities. The analytical laboratory was found on the ground floor. The mezzanine was used for the storage of retained samples. The microbiological laboratory was located on the 1st floor. LIMS was under implementation, and qualification should be reviewed during the next inspection. The procedure for labelling samples was reviewed. The following procedures, analytical methods, and records were reviewed:

- The SOP for receipt of samples of raw and packaging material at the laboratory
- The SOP for storage of temperature sensitive materials at the laboratory
- The analytical record, specifications and analytical methods for Tenofovir Disoproxil Fumarate

OOS

A procedure for handling out of specification test results in the laboratory was available. OOS results were registered in TrackWise and investigations had to be conducted. Examples of OOS investigations were reviewed.

Stability studies

Stability studies were carried out in accordance with a written procedure. The procedure described the conditions for stability studies of validation batches (i.e., accelerated, intermediate and long-term). According to the procedure at least one batch of each API manufactured during the year had to be placed in an on-going stability study. The Amino Salicylate (PAS) stability study (T:30±2°C, RH:75±5%) was reviewed in detail.

Any observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

11. Validation

A VMP was in place to provide the principles of validation. In general, production and laboratory equipment had to be qualified/calibrated prior to use and then after any significant change. Examples of production and laboratory equipment qualifications were reviewed.

HVACThe requalification of the HVAC system in the clean area of Block A- Module VII was also reviewed. The protocol and report were provided. The system supplied filtered air to the drying, milling, sifting & packing room, the corridor, the crystallization room, the washing room, and the change-II room. The following tests were performed:

- Air-velocity- air changes
- Filter integrity
- Air flow pattern
- Recovery
- Differential Pressure
- Viable and non-viable particles
- Temperature and Relative Humidity
- Sound level test

Any observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

12. Change control

Change management followed the instructions provided in a written procedure. Examples of change management reviewed during the inspection included:

- change in the name of a manufacturer/supplier of R-3-amino-1-butanol

- change in the frequency of sanitization of the PW system.
- Change in the calibration schedule of equipment of the PW system.
- Structural changes in Block A, including changes in HVAC.

Any observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

13. Rejection and re-use of materials

All rejected raw and packaging materials were appropriately labelled, segregated, and stored in a dedicated area. In most cases rejected materials were sent back to the suppliers. Finished products not meeting the specifications were either rejected or reprocessed/reworked after investigation and QA approval.

Reprocess, Rework and Recovery

The SOP (for reprocessing, reworking and recovery) was reviewed. The procedure adequately described the steps and defined the responsibilities for investigating a batch of material/intermediate/finished product that did not comply with specifications, developing a reprocess/rework batch record, uniquely identifying the process and batch, and carrying out additional controls, including stability studies. Reprocessing, reworking and recovery of the same material could only be performed twice. Examples of API reprocessing were reviewed.

Recovery of solvents, reactants, intermediates, or of the API was considered acceptable provided that appropriate processes were applied, and the recovered material met the established specifications. Recovered solvents could only be used for the same product, manufacturing stage and specific reaction step from which they were recovered. Specifications for fresh Methylene Chloride and recovered Methylene Chloride (Tenofovir Disoproxil Fumarate) were reviewed along with the Batch production and Control Record for recovered Methylene Chloride.

Any observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

14. Complaints and recalls

Customer complaints were registered in TrackWise and handled in accordance with a written SOP. Complaints were categorized as critical, major, or minor. Investigations had to be carried out, and complaints had to be closed out within 35 days. The 2022 list of complaints was made available and reviewed. Examples of complaint handling were reviewed.

Product recall followed the principles described in a written procedure. The SOP provided appropriate instructions on how to recall/remove products from the market in a timely manner. The responsibility of recalling was assigned to the site QA, the corporate quality head, the pharmacovigilance head, the regulatory head, and the marketing and distribution head.

The depth of the recall was categorized into 3 levels: customer/user level, retail level, and wholesale level.

Mock recalls were performed in accordance with an SOP. Different templates were used for domestic product recalls and export product recalls. A mock recall was performed annually (in case no recall had taken place in that year). The 2022 mock recall records were reviewed in detail.

Any observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

15. Contract manufacturers (including laboratories)

Production of the WHO APIs was not contracted out. Certain tests were contracted out to approved laboratories, and they were periodically audited.

Part 3	Conclusion – Inspection outcome
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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, *Macleods Pharmaceuticals Limited, Unit V*, located at *Plot No. 2209, CIDC, Sarigam, Dist. Valsad, State Gujarat, India 396155* was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines for APIs.

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
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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://www.who.int/publications/m/item/trs986-annex2>
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
<https://www.who.int/publications/m/item/annex-2-trs-957>
3. WHO guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report. Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 9.
Short name: WHO TRS 1010, Annex 9
<https://www.who.int/publications/m/item/trs1010-annex9>

4. 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
<https://www.who.int/publications/m/item/annex-3-trs-1033>
5. 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://www.who.int/publications/m/item/annex-4-trs-929>
6. WHO good practices for pharmaceutical quality control laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-seventh Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052), Annex 4.
Short name: WHO TRS No. 1052, Annex 4
<https://www.who.int/publications/i/item/9789240091030>
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://www.who.int/publications/m/item/trs957-annex3>
8. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty Second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8.
Short name: WHO TRS No. 1010, Annex 8
<https://www.who.int/publications/m/item/Annex-8-trs-1010>
9. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditioning 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://www.who.int/publications/m/item/trs1019-annex2>
10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
Short name: WHO TRS No. 1044, Annex 4
<https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/production/trs1044-annex4-technology-transfer-in-pharmaceutical-manufacturing.pdf>

11. WHO good manufacturing practices for sterile pharmaceutical products. Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
Short name: WHO TRS No. 1044, Annex 2
<https://www.who.int/publications/m/item/trs1044-annex2>
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://www.who.int/publications/m/item/trs943-annex3>
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://www.who.int/publications/m/item/trs961-annex2>
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://www.who.int/publications/m/item/trs981-annex2>
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://www.who.int/publications/m/item/annex-3-trs-981>
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
<https://www.who.int/publications/m/item/tr961-annex14>
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://www.who.int/publications/m/item/trs1019-annex3>
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

<https://www.who.int/publications/m/item/trs992-annex4>

19. 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://www.who.int/publications/m/item/trs961-annex9-modelguidanceforstoragetransport>

20. 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

<https://www.who.int/publications/m/item/trs992-annex5>

21. 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/trs-992-annex-6>

22. 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

<https://www.who.int/publications/m/item/annex-4-trs-1033>

23. 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

<https://www.who.int/publications/m/item/trs966-annex10>

24. 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**

Short name: WHO TRS No. 1010, Annex 10

<https://www.who.int/publications/m/item/trs1010-annex10>

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

<https://www.who.int/publications/m/item/annex-2-trs-1033>

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

<https://www.who.int/publications/m/item/trs-1025-annex-6>

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/m/item/trs-1025-annex-3-water-for-injection>

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/m/item/trs1025-annex4>

28. Good trade and distribution practices for pharmaceutical starting materials. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 6.

Short name: WHO TRS No. 996, Annex 6

<https://www.who.int/publications/m/item/annex-6-trs-996>

29. WHO guidelines for preparing a laboratory information file. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report* Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 13.

Short name: WHO TRS No. 961, Annex 13

<https://www.who.int/publications/m/item/trs961-annex13>

30. WHO good manufacturing practices for excipients used in pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-seventh Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052), Annex 1.

Short name: WHO TRS No. 1052, Annex 1

<https://www.who.int/publications/i/item/9789240091030>