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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	**Lupin Limited, Jammu**
Corporate address of manufacturer	Kalpatru Inspire 3rd Floor, Off Western Express Highway, Santacruz (East), *Mumbai 400055, India*
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Lupin Ltd EPIP, SIDCO Industrial Complex, Kartholi Bari Brahmana, 181 133 Jammu & Kashmir, India Latitude: 32.64536020 Longitude: 74.90480060 32.64536020,7 4.904800 60
Unit / block / workshop number	Manufacturing areas A & B
Inspection details	
Dates of inspection	5-8 April 2022
Type of inspection	Routine GMP inspection
Introduction	
Brief description of the manufacturing activities	The manufacturing facility is located at EPIP, SIDCO Industrial Complex, Kartholi, Bari Brahmana in the state of Jammu and Kashmir (Pin code: 181133). This is about 12 Km from the Jammu railway station and about 10 Km from the airport. The total plot area is 29609 square meters with an actual total built-up area of approximately 13900 square meters. The facility at Jammu is engaged in the manufacturing of Solid Oral Dosage (Tablets & Capsules) and Metered Dose Inhalers.
General information about the company and site	Lupin Ltd was founded in the year 1968 and is currently engaged in the manufacturing of Formulation, API and Biotechnology based products. Lupin has its R & D Facility, Lupin Research Park (LRP) at Pune and Aurangabad where research and formulation development are being performed. Lupin has its bulk drug manufacturing (API) facility at Tarapur (Maharashtra), Baroda (Gujarat), Indore, Mandideep (Madhya Pradesh), Vizag (in Andhra Pradesh), and Ankleshwar (Gujarat). The formulation facilities are situated at Verna (Goa), Pune, Aurangabad, Nagpur (Maharashtra), Mandideep, Indore (Madhya Pradesh), Jammu (Jammu & Kashmir) and Sikkim.

History	This was the fourth WHO PQ inspection of Lupin Limited, Jammu. The site was previously inspected in 2011, 2014, and 2018 and desk assessment in 2020. In addition, the site has been inspected by the State and Central Drug Authority of India.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Document Review included but was not limited to: - Organization chart - Quality risk management - Complaints and recalls - Documentation system - Job descriptions - Training - Change control - Deviation control - Annual product quality review - OOS investigations - Process validation - Cleaning validation - Quality risk management - Batch manufacturing records - Specifications and method of analysis - Stability studies - Electronic data and audit trail **Site areas visited:** - Manufacturing areas cover warehouse, sampling, dispensing, manufacturing area B (granulation, compression, coating and packaging), analytical laboratory, and microbiological laboratory. - Purified water system - Air handling units
Restrictions	None
Out of scope	The products manufactured outside the scope of WHO PQ were out of the scope of the inspection.
WHO products covered by the inspection	1. TB350 Linezolid Tablet, Film-coated 600mg 2. TB376 Moxifloxacin (hydrochloride) Tablet, Film-coated 400mg 3. TB068 Isoniazid/Rifampicin Tablet, Film-coated 75mg/150mg 4. TB070 Ethambutol hydrochloride/Isoniazid/Pyrazinamide/Rifampicin Tablet, Film-coated 275mg/75mg/400mg/150mg 5. TB177 Ethambutol hydrochloride Tablet, Film-coated 400mg 6. TB375 Isoniazid Tablet 300mg (under assessment)
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
APS	Aseptic process simulation

BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GMP	Good manufacturing practices
GPT	Growth promotion test
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IQ	Installation qualification
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MFT	Media fill Test
MR	Management review
NC	Non conformity
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis

RO	Reverse osmosis
SIP	Sterilization in place
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer
WFI	Water for injection

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

1. Pharmaceutical quality system

The company has established a quality management system (QMS) based on the requirement of national and international regulatory authorities. The quality and production departments operate independently under different leadership. The senior management demonstrated a commitment to the QMS including sufficient resources to implement and manage the QMS. Senior management also participates in the system through the conduct of periodic management review meetings.

Product quality review (PQR)

The SOP for the annual product quality review of drug products was available which provided guidance related to the purpose, scope, responsibility and procedure for the PQR. The procedure also provided guidance on the process capability index (CpK) which is performed using a minimum of 10 batches. The site maintains the APQR planner of all products distributed within a year from the date of their approval. A separate procedure for the operation of Minitab software was in place. The PQRs of the selected products were reviewed

Change controls

Change control procedure was discussed. The procedure was applicable to document changes as well as other areas such as equipment, process, and personnel. The changes are classified into permanent and temporary changes and then further sub-classified into major and minor. The company used Caliber QAMS (Quality Assurance Management System) for handling changes as well as other QMS modules (deviations, complaints, OOS, LIR, CAPA, and management notification) are handled through QAMS. The staff members have access privileges to initiate a change. The changes were categorised as permanent and temporary and classified into major and minor. Some of the change controls were reviewed and noted that FMEA (RPN) was used to assess the risk.

Deviations

Handling of deviations procedure was discussed. The deviations were categorised as critical, major and minor based on the impact assessment. An initial impact assessment was performed by the QA to categorise the deviations. The deviations were tracked and trended using QAMS wherein trending was performed quarterly.

Quality risk management (QRM)
The SOP on QRM was discussed. The procedure covered risks identified prospectively and retrospectively by the site. The SOP was supported with risk assessment tools such as FMEA, FTA, HACCP. The QRM for Isoniazid 300mg tablets was discussed which was performed as part of the introduction of a new product at the site.

Management review
The SOP for the management review of the quality metrics was available. The corporate management team (QA Head, QC Head, and production Head) was responsible for the monthly management review. Since the last inspection (2018), the management now keeps the records of the minutes with the key information discussed. Action plans and timelines were defined. This activity was found to follow the requirements of the WHO guidelines, including the products, processes and systems investigated.

The deficiencies noted from the pharmaceutical quality system section have been addressed satisfactorily and the same will be verified during future PQ inspections.

2. Good manufacturing practices for pharmaceutical products
Basic principles of good manufacturing practices were described and implemented. Manufacturing processes were generally adequately defined and documented in BMRs and BPRs. Required resources were available, including adequate premises, equipment, and utilities. Appropriately qualified personnel were employed.

Lupin Limited, Jammu has a shared/multipurpose manufacturing facility. The facility produces several products of different therapeutic areas in oral solid dosage form and metered dose inhalers. As a shared manufacturing facility, the company had implemented containment measures to ensure contamination and cross-contamination issues, especially since the last WHO PQ inspection.

The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

3. Sanitation and hygiene
Premises and equipment were generally cleaned according to established procedures.

The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

4. Qualification and validation
Site validation master plan dated was reviewed which was prepared following the SOP on qualification/validation planning & organization issued by the Corporate QA team. The site VMP was reviewed once every two years and whenever any changes are made. The VMP included all the equipment, instruments, areas and utilities required to be qualified and validated during the year 2022. Separate departments were responsible for the execution of validation activities. The process validation of the WHO product (under assessment) and process performance qualification for some of the prequalified products were reviewed.

The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

5. Complaints

The SOP or handling of market complaints about drug products was discussed. Complaints were categorized into 4 levels: critical (serious health risk), major (risk of illness or mistreatment), minor (impact on product quality, safety and/or efficacy), and adverse drug event (ADE). The QAMS software was used for complaints handling. In general, it was noted that the causes of quality defects were appropriately investigated, with appropriate corrective measures taken. CAPAs were adequately tracked in the QAMS system, which was not the case during the last 2018 inspection.

6. Product recalls

The SOP for recall/Market withdrawal of drug products was reviewed. There were 3 levels of recalls: consumer or user level (patients, physicians, hospitals), retail level (pharmacies) and wholesale level (distributors). The initiation of a drug product batch was under the responsibility of the Head of QA. The execution of market recall from overseas was also reviewed. The SOP describes the protocol for mock recall.

7. Contract production, analysis and other activities

This section was not inspected due to time constraints

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

Self-inspection procedure for the site was in place. The self-inspection was performed once every 6 months covering all departments within the site. The annual planner was prepared by the QA every year identifying areas/departments to be audited. An execution planner was available to provide the current status of self-inspection. From the review of the executed planner, it was noted that independent personnel were appointed as auditors for auditing different departments. The SOP on self-inspection also stipulated that audit members should be independent of those having direct responsibility for the areas being audited. A department-wide checklist was used for recording audit findings. A list of qualified auditors was maintained for 2022.

The vendor qualification procedure was discussed which described how vendors should be qualified (new) and requalified (existing) using the SAP system. The vendors are requalified every three years to five years based on the type of materials (e.g. API versus secondary packaging materials, excipients etc). Based on the qualification of vendors, a scoring was assigned and requalification. The vendor qualification is coordinated by CQA. A list of 55 approved auditors (CQA and site identified) was available as part of the procedure. The company has created a new vertical within the company responsible for auditing vendors and Lupin's sites. This is to ensure there is independency and no conflict of interest.

The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

9. Personnel

The SOP for Organograms Lupin Limited was reviewed. This document was an annex of the SOP for job responsibility. The job responsibilities of the key personnel were reviewed. In general, the job

descriptions, responsibilities and duties of the key personnel appeared to be adequately written and implemented and following the WHO guidelines, which was not the case during the last 2018 inspection.

10. Training

The SOP for the training of personnel was discussed. There were different types of training organised by the company:

- induction training,
- CGMP training,
- functional training,
- job-related training,
- competency-based "just in time" training,
- remedial training and
- self-development training.

The 2022 and 2021 training schedules were available for every activity, as well as individual training records. In general, the training program was found adequate.

11. Personal hygiene

Personnel gowning procedure was available. The gowning was changed every day.

The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

12. Premises

Ground floor layout housed manufacturing areas A, B and C, C is dedicated to Metered Dose Inhalers (MDI) whereas A and B are used for all OSD products. Besides manufacturing activities, the ground floor housed the incoming raw material store and finished goods store.

The layout of the first floor housed a service area for AHUs, PW generation & distribution, QC, microbiology lab, QA office, document storage and stability chambers.

The company stored the solvents used for the coating of the tablets in a dedicated and separated area (G158). This area was inspected. Different kinds of solvents were kept at the time of inspection:

- Methylene chloride
- Isopropyl alcohol
- Methanol
- Absolute alcohol

The inventory of the solvents was kept and managed electronically. All the metallic drums were connected to the ground. The area appeared appropriately ventilated. The management of this activity was found acceptable.

Microbiology laboratory visit: see section 17 of this report.

In general, the premises (material and people flow) were found to be adequate.

13. Equipment

The equipment used in the manufacturing, processing, and packaging was of appropriate design. The equipment was placed in a suitable location to facilitate operations for their use, cleaning, and maintenance.

The utilities such as the purified water system, compressed air and air handling units were inspected. The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

14. Materials

Incoming materials (active, excipients, packaging materials) were received through five receiving bays (solid materials, packaging materials, liquids). The receiving bays were equipped with a trap station used for rodent bait. The warehouse was equipped with three sampling booths for excipients and actives and sampling was carried out under RLAF. The warehouse had three dispensing booths two for inactive substances and one for active substances. The dispensing area was equipped with sodium vapour lamps for light-sensitive materials. At the time of the inspection, there was no sampling and dispensing activities were being carried out.

The primary packaging materials were stored in a controlled environment. The warehouse management system (WMS) was used for material management. The manufacturer was recommended to store incoming materials at specific storage conditions instead of room temperature or ambient temperature. The finished goods store was found clean and tidy at the time of inspection. The WHO PQ products were stored below 30°C and awaiting dispatch to USAID, Global Fund and Malaria Consortium.

Rejected and returned materials area was located in a dedicated and separate part of the warehouse, hence were kept at the same temperature and humidity conditions.

The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

15. Documentation

In general, documentation was designed, prepared, reviewed, and distributed according to a documented procedure. Quality system documents were regularly reviewed and kept up to date. Approved, signed and dated testing procedures and specifications were available for starting and packaging materials and for finished products.

The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

16. Good practices in production

Clean areas for the manufacture of non-sterile OSD products were classified (ISO 8) according to the expected required characteristics of the environment. Separate change rooms were provided for visitors and staff members.

Some of the production and packaging activities were in operation during the inspection. Most of the production and packaging operations were carried out using open systems and processes. In the production area, adequate measures were not taken to contain dust generated when materials, in-process products and finished products were handled and transferred from one unit operation to another unit operation. From the visit to the manufacturing area, it appeared that the manufacturer has the practice to move equipment and instruments from one production area to another area. Such practices will lead to a risk of contamination and cross-contamination. The IPQC was briefly visited and noted that in-process samples were tested in different manufacturing areas confusing their traceability (whether manufacturing area A or B was used). From the visit to the primary packaging area, it was found that adequate measures were taken to contain the generation of dust when blistering operations were carried out. This change was made following the last WHO PQ inspection in 2018.

The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

17. Good practices in quality control

The laboratory was divided into four sections:

1. QC Instruments section
2. Wet Chemistry Lab
3. Microbiology Section
4. Stability Study Section

The analytical balances were calibrated and verified monthly and daily respectively. The monthly calibration included accuracy, sensitivity, repeatability and eccentricity whereas verification included four-point verification. The standard weights were calibrated against NABL. The chromatographic data systems were connected with servers and appropriate procedures were in place for access controls and management of the privileges.

<u>Out-of-specifications results</u>

The SOP for the handling of out-of-specification results was discussed. The SOP describes the investigation process. Phase I is the laboratory investigation, if no error (analyst, method, equipment, calculation, etc) was identified, Phase II (manufacturing investigation) was initiated. The decision tree was discussed.

Microbiology laboratory
The microbiological laboratory was located on the first floor of the building. The laboratory performed the following testing:

- Microbiological limit test on raw materials, and finished products, upon the requirements of the dossier
- Sterility test on the media
- Environmental monitoring
- Purified water testing
- Cleaning validation
- Compressed air testing

The laboratory was comprised of an airlock, a bio testing room, an incubation room, an autoclave room, and a washing room. All the rooms appeared to be appropriately segregated and organized regarding the activities performed 2 dedicated AHUs were ventilating the area.

Working and reference standards: The reference standards were kept either in a refrigerator or kept at room temperature, depending on their source and their usage.

Packaging material laboratory
The packaging material testing laboratory was briefly visited. The pinhole tester was used for checking pinholes on foils. The pinhole tester was in-housed assembled equipment which did not require any calibration or verification.

The deficiencies noted from this section have been addressed satisfactorily and the same will be verified during future PQ inspections.

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, ***Lupin Ltd,*** located at ***EPIP, SIDCO Industrial Complex, Kartholi Bari Brahmana, Jammu & Kashmir, India*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines.

All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the WHOPIR were addressed by the manufacturer, to a satisfactory level, prior to the publication of the WHOPIR

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

Part 4	List of WHO Guidelines referenced in the inspection report

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-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***
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12. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-first Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. ***Short name: WHO TRS No. 943, Annex 3***
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13. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2.
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Short name: WHO TRS No. 981, Annex 2
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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
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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***
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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***
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20. WHO Recommendations for quality requirements when plant – derived artemisin is used as a starting material in the production of antimalarial active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 6
Short name: WHO TRS No. 992, Annex 6
https://www.who.int/publications/m/item/who-recommendations-for-quality-requirements-when-plant-derived-artemisinin-is-used-as-a-starting-material-in-the-production-of-antimalarial-active-pharmaceutical-ingredients---trs-992---annex-6

21. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4. ***Short name: WHO TRS No. 1033, Annex 4***
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22. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
Short name: WHO TRS No. 996, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

23. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 10.
Short name: WHO TRS No. 1010, Annex 10
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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**
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25. Points to consider when including Health-Based Exposure Limits in cleaning validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 2. **Short name: WHO TRS No. 1033, Annex 2**
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26. Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 6. **Short name: WHO TRS No. 1025, Annex 6**
9789240001824-eng.pdf (who.int)

27. Production of water for injection by means other than distillation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 3. ***Short name: WHO TRS No. 1025, Annex 3***
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28. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4. ***Short name: WHO TRS No. 1025, Annex 4***
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