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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	**Laurus Labs Limited**
Corporate address of manufacturer	2nd Floor, Serene Chambers Road No.: 7, Banjara Hills Hyderabad-500034 Telangana India
Inspected site	
Name & address of inspected manufacturing site if different from that given above	**Laurus Labs Limited Unit-2** Plot No: 19, 20 & 21 Western Sector APSEZ, Atchutapuram Visakhapatnam - 531011 Andhra Pradesh India
Unit / block / workshop number	MB01
Inspection details	
Dates of inspection	14 - 18 February 2022
Type of inspection	Real-time remote assessment
Introduction	
Brief description of the manufacturing activities	Production and quality control of oral solid dosages including tablets and capsules, APIs, and intermediates.
General information about the company and site	Laurus Labs Limited, formerly known as Laurus Labs Private Limited, is headquartered in Hyderabad, Telangana, India. At the time of the real time remote assessment, there were three manufacturing blocks (MB) in Unit 2. MB01 Drug Product Block (Oral solid dosage forms - tablets and capsules) was in the remote assessment scope. No penicillin, cephalosporin products and high potent products are manufactured on the site.
History	This is the third WHO inspection of the site with the first on-site inspection held in March 2017 and desk assessment in January 2021. Unit 2 OSD facility had been inspected by US FDA in November 2019 with positive outcome. The site is inspected by CDSCO & DCA on a regular basis.

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Pharmaceutical quality system Production block MB01 QC including chemical and microbiological laboratories Personnel Utilities Materials
Restrictions	The inspection was restricted to the production of the product listed in the inspection scope. Access to production and quality control was limited due to the remote assessment and unstable Wi-Fi connection.
Out of scope	Products out of scope of WHO PQ
WHO products numbers covered by the inspection	1. HA679 Tenofovir disoproxil fumarate Tablet, Film-coated 300mg 2. HA707 Dolutegravir (Sodium)/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg 3. HA709 Darunavir Tablet, Film-coated 400mg 4. HA710 Darunavir Tablet, Film-coated 600mg 5. HA711 Darunavir Tablet, Film-coated 800mg 6. HA717 Emtricitabine/Tenofovir disoproxil fumarate Tablet, Film-coated 200mg/300mg 7. HA718 Dolutegravir (Sodium) Tablet, Film-coated 50mg 8. HA727 Efavirenz/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 600mg/300mg/300mg 9. HA732 Efavirenz/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 400mg/300mg/300mg 10. HP027 Daclatasvir (dihydrochloride) Tablet, Film-coated 30mg 11. HP028 Daclatasvir (dihydrochloride) Tablet, Film-coated 60mg
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
FEFO	First Expiry First Out
FIFO	First in First Out

FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GMP	Good manufacturing practices
GPT	Growth promotion test
HDPE	High density polyethylene
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
MR	Management review
NC	Non conformity
NCA	National control authority
NCL	National control laboratory
NCR	Non conformance report
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

1. Pharmaceutical quality system

The quality management system was generally well established, documented and implemented. The site organizational structure was presented and was generally acceptable. Quality-related activities were defined and documented. The quality assurance department was independent from production. The persons authorized to release products were specified.

Product Quality Review (PQR)

SOP for Product Quality Review was reviewed. According to the SOP, the PQR report for commercialized drug products was prepared annually - Calendar year. At the time of the remote assessment, the number of batches produced for the PQ relevant products in the year 2019, 2020 and 2021were summarized and provided for review.

APQRs for year 2021 were under preparation and were not yet available at the time of this remote assessment. The PQR report was required to be reviewed and approved within 90 days from the due date of the review period i.e., on or before 31st March.

The following APQRs were reviewed:

1. Product Name: Emtricitabine and Tenofovir disoproxil fumarate Tablets 200mg/300mg (WHO HA717)
   Review period: January 2020 to December 2020
   The data contained in the PQR was reviewed.
   - Batches manufactured and released.
   - Deviations, OOS, permanent change controls and temporary change controls were reported. There was no batch rejection, return and complaint during the review period. Process validation was performed on 3 batches where the batch size was increased.

2. Product Name: Dolutegravir, Lamivudine and Tenofovir disoproxil fumarate Tablets 50mg/300mg/300mg (WHO HA707)
   Review period: January 2020 to December 2020
   The data contained in the PQR was reviewed.
   - Batches manufactured and released.
   - Deviations, OOS, OOT, permanent change controls and temporary change controls were reported. There was no batch rejection, return and complaint during the review period. Process validation was performed in 2020 for commercial batch for new line of equipment in Dolutegravir part.

Management review

SOP for management review was checked. The content and frequency of the management review was stipulated in the procedure. Minutes of the Management Meeting dated July 2021 for Laurus Unit 2 was reviewed and acceptable.

Deviations

SOP for handling of deviation was checked. Deviations classified as critical, major and minor. Deviations were handled in an electronic Quality Assurance Management System (eQAMS) Module. Deviations were required to be closed within specified working days from the initiation date. Trending was required to be performed. A consolidated report was required to be prepared at the end of the year with a comparison of the data of the previous years. The deviation trends were noted in the Management Review (January to June 2021). A deviation report was reviewed during the inspection.

CAPAs

SOP for corrective and preventive action was checked. CAPAs were required to be closed within specified working days from the date of initiation. If an extension was required, QA authorised the extension. CAPA effectiveness was to be reviewed by QA. The CAPAs' trend was noted in the Management Review (January to June 2021).

Change Control

SOP for change control system was checked. Changes were classified as major and minor, as well as permanent and temporary changes. Several change controls were reviewed during the inspection.

Out of Specifications (OOS)

SOP for handling of out of specifications was checked. Investigation to determine the root cause of OOS results carried out in two phases. The OOS and OOT trends were noted in the Management Review (January to June 2021). Several OOS investigation reports were checked during the inspection.

Product release

SOP for product release of FPP was reviewed. A check list was available to document the key elements required to be reviewed. No objectional comments was made.

2. Good manufacturing practices for pharmaceutical products

Good manufacturing practices were generally implemented. Necessary human and physical resources were provided for the current operational level of FPP activity. Manufacturing processes were generally adequately defined. The manufacturing processes follow procedures as defined and documented in the BMRs and BPRs. Product and processes were monitored, and the results were checked as part of the approval process for batch release. The personnel are appropriately qualified and adequate training was conducted.

It was noted that 10 out of 11 PQed products were approved after the last on-site inspection conducted in 2017. Details of their production and quality control should be reviewed in future on-site inspection as access to manufacturing facility, product production and its visibility were limited during the remote inspection, as well as time difference between India and where inspectors located.

3. Sanitation and hygiene

Premises and equipment in the FPP production area appeared to be maintained at a satisfactory level of cleanliness at the time of the remote assessment. Personal hygiene and sanitation appeared satisfactory.

4. Qualification and validation

Process validation

Process validation was performed according to written procedures and protocols. The following process validation documents and BMRs of validation batches were reviewed:

- Process Validation Protocol for Daclatasvir Tablets common Blend
- Process Validation Report for Daclatasvir Tablets common Blend
- Process Validation Protocol for Daclatasvir Tablets 30mg
- Process Validation Report for Daclatasvir Tablets 30mg
- Process Validation Protocol for Daclatasvir Tablets 60mg
- Process Validation Report for Daclatasvir Tablets 60mg
- Executed BMR for Daclatasvir Tablets Common Blend
- Executed BMR for Daclatasvir Tablets 30mg
- Executed BMR for Daclatasvir Tablets 60mg

Equipment qualification

A performance qualification protocol and report for tablet visual inspection equipment and an SOP for acceptable quality level inspection were reviewed during the inspection.

Cleaning validation

Production equipment in MB01 was not dedicated. The following cleaning validation documents were spot checked:

- Cleaning Validation Protocol for Dolutegravir Tablets 50mg
- Cleaning Validation Report for Dolutegravir Tablets 50mg
- A cleaning validation monitoring protocol

The confirmation and verification of the cleaning effectiveness for product change-over were discussed. The requirement and data were not reviewed in detail due to time constraints and should be followed up in future on-site inspection.

5. Complaints

SOP for handling of drug product market complaints was checked. Market complaint was classified as critical, major and minor based on nature and severity. Target working days for closure was stipulated in the procedure. A complaint investigation report regarding Tenofovir Disoproxil Laurus 245 mg film-coated tablets was reviewed.

6. Product recalls

Product recall

SOP for handling of product recall was checked. Recalls may be conducted on the company's own initiative, by Drug Regulatory Authority notification or by Drug Regulatory Authority's order under statutory requirement. Causes would trigger a product recall, recall classification and execution of the product recall were specified in the recall procedure. No recalls to date.

SOP for Product recall and a mock recall report issued in December 2020 were available and reviewed.

Product return

SOP for handling of returned finished goods was spot checked and was not inspected in detail due to time constraints.

7. Contract production, analysis, and other activities

No manufacture was contracted out. Some QC testing was contracted out to labs in other Laurus Units.

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

SOP for internal audits (self-inspection) was checked. The frequency of internal audits was specified. The self-inspection schedule for 2020 and 2021 (as at 30-07-2021) was available. Internal Audits performed in March 2021was checked during the inspection.

Vendor management

The procedure for vendor qualification procedure for raw materials and packaging materials used in dosage forms was in place. A Vendor Audit report and Quality Technical Agreement were reviewed.

9. Personnel

Total number of personnel at Laurus Labs Unit 2 was 928 according to the company presentation. 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. Several job descriptions of employees from QA, QC and Engineering and Maintenance department were checked during the inspection.

10. Training

SOP for employee training was checked. The SOP applied to all employees who were deployed in all kinds of developmental, manufacturing, and testing activities. This procedure was applicable for training performed manually and using the electronic system. Employee Training record was maintained. Several employees training records were checked and found to be acceptable.

11. Personal hygiene

Personnel hygiene requirements were documented in an SOP for personal hygiene practices in plant. Staff observed in Grade D cleanrooms of production areas were dressed in appropriate protective clothing.

12. Premises

MB01 is multi-product not dedicated OSD facility. The classified areas were monitored for temperature, relative humidity, and pressure differentials with BMS system for environmental control. A virtual tour for remote assessment was conducted. The following areas were covered:

- Warehouses
- Manufacturing
  - The layout of the facilities allowed for a logical flow from dispensing to final packaging.
- Utilities
  - Purified Water System
  - HVAC
- QC laboratories including chemistry and microbiology laboratory were separated from production areas.

Purified water (PW)

There were two water systems on the site used separately for API and FPP production. Purified water was produced from raw water through pre-treatment system then by double RO followed by EDI. Purified water system generation and distribution diagram was reviewed. The design was suitable to produce PW for FPP production.

13. Equipment

Design and construction

Equipment installed in MB01 was multi-purpose and each piece of equipment had a unique identification number. In general, the equipment, remotely viewed, appeared to be of suitable design and construction for the allocated process.

Equipment maintenance and cleaning

The equipment viewed during the remote inspection appeared to have been suitably maintained and in good condition. Equipment status labels were available. Cleaning procedures and records were available, and spot checked.

Equipment calibration

The following SOPs were checked:

- SOP for calibration of analytical equipment
- SOP for calibration of measuring and testing instruments
- SOP for calibration of analytical equipment
- SOP for calibration of measuring and testing instruments

Instrument calibration schedule was prepared annually for measuring instruments, including master instruments and spare instruments.

Computer System (CS)

Computerized systems were currently used in quality management, warehouse and in production. The CS validation and data management was not reviewed in detail due to time constraints and limitation of remote assessment.

14. Materials

Vendor approval

SOP for vendor qualification procedure for raw materials used in dosage forms was checked.
This procedure was applicable for the identification, qualification, and requalification of vendors and included the procuring of APIs/Excipients/Solvents/Primary Printed/Secondary/Tertiary Packaging materials, which were to be used in the manufacturing of dosage forms, as per cGMP regulations.

FG Warehouse

The following documents were checked:

- SOP for receipt, storage and dispatch of finished goods
- SOP for transport validation
- Temperature mapping protocol and report for Warehouse WH01
- Transport validation protocol and report for Tenofovir Disoproxil Fumarate Tablets 300 mg

15. Documentation

The documentation system was paper based and few electronic systems like eQAMS , LMS, DMS controlled by QA department. In general, documentation was designed, prepared, reviewed, and distributed according to documented procedures for preparation of standard operating procedure and for document control.

Batch numbering system was managed according to SOP for batch numbering system for drug products. Batch Manufacturing Records (BMRs) were retained for each batch processed. Batch Manufacturing record for Dolutegravir, Lamivudine and Tenofovir Disoproxil Fumarate Tablets reviewed was generally acceptable.

16. Good practices in production

The manufacturing processes were performed and recorded according to instructions in the Batch Production Records. The production of HA707 Dolutegravir (Sodium)/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg batch no. 220291 was in operation at the time of remote inspection. Manufacturing records of the products under processing spot checked and found acceptable.

The IPC testing (e.g., leak test, tablet weight) was performed in the IPC laboratory, located within the processing area, were inspected, and found acceptable.

17. Good practices in quality control

A virtual tour of the laboratories was conducted, which included both chemistry and microbiology laboratories. QC responsibilities were defined in SOP for responsibilities of quality control. Based on the area of work assigned, analysts/microbiologists are required to perform tests listed in respective modules.

SOP for evaluation of analytical/microbiology laboratory personnel which described the training required for laboratory personnel was reviewed.

Testing of starting materials and finished products

QC testing was conducted as specified in the relevant specifications and according to documented test methods. The sample receiving, and distribution logbook, reserve sample logbooks were spot checked.

SOP for sampling of raw materials (API and excipients) and SOP for reduce testing of raw materials (API and excipients) used in dosage forms were reviewed and discussed.

Stability monitoring of FPPs

A range of stability chambers were available at the QC lab. The following stability data were checked. No objectional comments was made.

- Stability protocol and Daclatasvir Tablets 30/60 mg
- Daclatasvir tablets 30 mg Stability Summary report

Reserve/retention samples

There was a designated temperature-controlled area for storage of retention samples.

Part 3	Initial conclusion – Inspection outcome

Based on the previous WHO inspections and on the GMP evidence received and reviewed, it is considered that a desk assessment is acceptable in lieu of a WHO onsite inspection. The site ***Laurus Labs Limited, Unit-2,*** located at ***Plot No: 19, 20 & 21, Western Sector APSEZ, Atchutapuram, Visakhapatnam - 531011, Andhra Pradesh, India*** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

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 GMP 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://www.who.int/docs/default-source/medicines/norms-and-standards/guidelines/production/trs1010-annex8-who-gmp-heating-ventilation-airconditioning.pdf?sfvrsn=c77698e2_0

6. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4.
   Short name: WHO TRS No. 937, Annex 4
   https://digicollections.net/medicinedocs/documents/s20108en/s20108en.pdf

7. WHO good practices for pharmaceutical quality control laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1.
   Short name: WHO TRS No. 961, 957), Annex 1
   https://digicollections.net/medicinedocs/documents/s18681en/s18681en.pdf

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

9. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 6.
Short name: WHO TRS No. 961, Annex 6
https://digicollections.net/medicinedocs/documents/s19959en/s19959en.pdf

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7.
Short name: WHO TRS No. 961, Annex 7
https://digicollections.net/medicinedocs/documents/s18677en/s18677en.pdf

11. Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9. ***Short name: WHO TRS No. 961, Annex 9***
https://digicollections.net/medicinedocs/documents/s18683en/s18683en.pdf

12. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-first Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. ***Short name: WHO TRS No. 943, Annex 3***
https://digicollections.net/medicinedocs/#d/s21438en

13. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2.
Short name: WHO TRS No. 961, Annex 2
https://digicollections.net/medicinedocs/documents/s18682en/s18682en.pdf

14. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2.
Short name: WHO TRS No. 981, Annex 2
https://digicollections.net/medicinedocs/#d/s20177en/

15. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3.
Short name: WHO TRS No. 981, Annex 3
https://digicollections.net/medicinedocs/#d/s20175en/

16. WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14.
Short name: WHO TRS No. 961, Annex 14
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

17. Good Manufacturing Practices: Guidelines on validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3. ***Short name: WHO TRS No. 1019, Annex 3***
https://digicollections.net/medicinedocs/documents/s23697en/s23697en.pdf

18. WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4. ***Short name: WHO TRS No. 992, Annex 4***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

19. WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5. ***Short name: WHO TRS No. 992, Annex 5***
Essential Medicines and Health Products Information Portal (digicollections.net)

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

21. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4. ***Short name: WHO TRS No. 1033, Annex 4***
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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
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

24. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditionning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-third Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1019), Annex 2. **Short name: WHO TRS No. 1019, Annex 2**
https://digicollections.net/medicinedocs/documents/s23699en/s23699en.pdf

25. Points to consider when including Health-Based Exposure Limits in cleaning validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 2. **Short name: WHO TRS No. 1033, Annex 2**
9789240020900-eng.pdf (who.int)

26. Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 6. **Short name: WHO TRS No. 1025, Annex 6**
9789240001824-eng.pdf (who.int)

27. Production of water for injection by means other than distillation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 3. ***Short name: WHO TRS No. 1025, Annex 3***
https://www.who.int/publications-detail/978-92-4-000182-4

28. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4. ***Short name: WHO TRS No. 1025, Annex 4***
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