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Prequalification Unit Inspection Services
WHO PUBLIC INSPECTION REPORT
of the FPP manufacturer

Part 1	**General information**
Manufacturers Details	
Company information	
Name of manufacturer	Micro Labs Limited
Corporate address of manufacturer	27, Race Course Road Bangalore-560 001. India
Contact person	Rajesh Kshirsagar, Chief Operating Officer rajeshk@microlabs.in
Inspected site	
Address of inspected manufacturing site if different from that given above	Micro Labs Limited – ML-08 15/A, 2nd Phase, Kumbalgodu Industrial Area, Bangalore 560 060, India
Unit / block / workshop number	All areas inspected. Facility dedicated to manufacture of Rifampicin containing products.
Manufacturing license number	KTK/25/449/2000
Inspection details	
Dates of inspection	01-05 August 2022
Type of inspection	Routine re-inspection following refurbishing and recommissioning of plant
Introduction	
Brief summary of the manufacturing activities	Manufacturing and quality control of non-sterile oral solid dosage forms – Tablets dedicated to Rifampicin containing products.
General information about the company and site	Micro Labs Limited was established in 1973 with the Kumbalgodu manufacturing facility situated at the Kumbalgodu Industrial Area within Bangalore, starting operations in the year 2009. During the latter part of 2018, a decision was made to refurbish the facility to exclusively manufacture a range of anti-TB combination product containing Rifampicin. Non-Rifampicin containing products previously manufactured at the facility were transferred to other Microlabs manufacturing sites. The upgrade required the installation of new processing equipment, significant internal rebuilding of the facility, provision of new HVAC units and a new water plant as well as all supporting systems. The facility was shut down in May 2019 with the renovations and major validation activities completed in 2021. A comprehensive facilities start up report was completed prior to the phased commencement of submission batches using the small and

	medium scale manufacturing equipment. At the time of the audit in August 2022, the larger commercial scale equipment had been fully installed and qualified up to the OQ stage and hence could not be fully evaluated.
History	The site had previously been inspected by the WHO inspection team in 2011, 2012, 2014, 2015 and 2018.
Brief report of inspection activities undertaken	On-site GMP inspection conducted following refurbision of the site.
Areas inspected	The inspection covered all areas of the WHO GMP requirements and entire plant visited.
Restrictions	Not Applicable
Out of scope	Not Applicable
WHO product numbers covered by the inspection	TB223 Ethambutol (hydrochloride) /Isoniazid/ Pyrazinamide/Rifampicin Tablet, Film-coated 275mg/75mg/400mg/150mg

Abbreviations

AHU	air handling unit
ALCOA	attributable, legible, contemporaneous, original and accurate
API	active pharmaceutical ingredient
APQR	annual product quality review
BDL	below detection limit
BMR	batch manufacturing record
BPR	batch packaging record
CAPA	corrective actions and preventive actions
CC	change control
CFU	colony-forming unit
CoA	certificate of analysis
CpK	process capability index
DQ	design qualification
EM	environmental monitoring
FAT	factory acceptance test
FBD	fluid bed dryer
FMEA	failure modes and effects analysis
FPP	finished pharmaceutical product
FTA	fault tree analysis
FTIR	Fourier transform infrared spectrometer
GC	gas chromatograph
GMP	good manufacturing practice
HACCP	hazard analysis and critical control points
HPLC	high-performance liquid chromatograph
HVAC	heating, ventilation and air conditioning
IR	infrared spectrophotometer
IQ	installation qualification
KF	Karl Fisher
LAF	laminar air flow
LIMS	laboratory information management system
LoD	limit of detection

LOD	loss on drying
MB	Microbiology
MBL	microbiology laboratory
MF	master formulae
MR	management review
NMR	nuclear magnetic resonance spectroscopy
NRA	national regulatory agency
OQ	operational qualification
PHA	process hazard analysis
PM	preventive maintenance
PpK	process performance index
PQ	performance qualification
PQR	product quality review
PQS	pharmaceutical quality system
QA	quality assurance
QC	quality control
QCL	quality control laboratory
QRM	quality risk management
RA	risk assessment
RCA	root cause analysis
SOP	standard operating procedure
TAMC	total aerobic microbial count
TFC	total fungi count
TLC	thin layer chromatography
URS	user requirements specifications
UV	ultraviolet-visible spectrophotometer

Part 2	Brief summary of the findings and comments (where applicable)

1. Pharmaceutical quality system

A formal documented system for quality assurance was in place, with procedures covering key quality elements. Operations were specified in a written form and GMP requirements were essentially being met. Regular monitoring and reviews of the quality of pharmaceutical products were being conducted according to documented schedules and procedures. The Quality Unit was divided into QA and QC, which were managerially separate to the production department.

Product quality review (PQR)

The written procedure for PQRs was available for review. The SOP specified the review of API, in-process and finished product test results, OOS batches, deviations, changes, stability monitoring, complaints and recalls etc with abnormal observations to be investigated, impact assessment conducted and trending to be conducted based on critical parameters.

Management review

Management review procedure was available and was performed at both corporate and site level at specified time intervals.

Regulatory feedback

SOP, handling and sharing of data/document with Regulatory Affairs, QAGN: 038/A was implemented since the previous inspection. The SOP addressed appropriate feedback from the manufacturer to Corporate Regulatory Affairs to allow for sharing of data to obtain required regulatory approval.

OOS investigation

Corporate SOP on OOS investigation, was available and implemented at site. Following review of the SOP, no major concerns were identified. The procedure provided for the identification of 3 levels of investigation, Phase I, II, III and trending. During the inspection OOS investigations, recorded during the period July 2021 to June 2022 were reviewed.

Data Integrity

A Data Integrity Policy signed by senior management was communicated across the facility which was supported by the applicable SOP and included aspects of management's approach to data governance, requirements for data integrity risk assessments and associated controls and was supported by the computer validation protocols which had addressed many of the ALCOA+ principles during qualification of automated systems.

Risk Assessment

A comprehensive cross contamination risk assessment was prepared in support of the upgraded facility which addressed the high-level effectiveness of the facility design and operational controls.

Change Control

Following the decision to refurbish the facility, the decision was recorded in appropriate CAPA which was then supported through a series of risk assessments and change controls. Comprehensive facilities start up report was completed prior to the phased commencement of submission batches using the small and medium scale manufacturing equipment.

2. Good manufacturing practices for pharmaceutical products

Since the last inspection, the site was refurbished with the aim to manufacture exclusively a range of anti-TB combination product containing Rifampicin. The facility was shut down in May 2019 with the renovations and major validation activities completed in 2021. The inspection confirmed that manufacturing processes were defined and documented with Good manufacturing practices generally implemented and followed. Qualification and validation activities were performed. Manufacturing processes and batch manufacturing records were available for review. The upgrade included the installation of new processing equipment, significant internal rebuilding of the facility, provision of new HVAC units and a new water plant as well as all supporting systems.

3. Site sanitation and hygiene

Premises were maintained at an acceptable level of cleanliness. The company had standard operating procedures in place as the basis for its approach to personal hygiene and sanitation in its production facility. Gowning colour coding was used to identify responsibilities and area of work.

4. Qualification and validation

Validation was governed by the site Validation Master Plan which was supported by validation SOP's for each validation sub category.

Computer System Validation

The validation of computerized systems was governed by a Computer System Validation Policy SOP: which included a list of "GxP" systems on site together with key system details and the status of validations and periodic reviews. A similar list was presented for all the Corporate IT systems used on site.

The qualification and validation reports for the training system and subsequent periodic reviews were comprehensive and well documented and were supported by risk assessments prior to major changes. Validation of the computerized control systems for the granulator and fluidized bed dryer was performed.

The site had a limited number of non-equipment related software systems installed at the time of the inspection, with some identified systems under validation and implementation.

Cleaning Validation

Detailed step wise cleaning instructions and photographs were available for three levels of cleaning for each production room and piece of equipment which were supported by check lists and cleaning logs.
The identification of worst-case molecules and maximum allowable carry over for the production equipment included estimates of the PDE values and potential toxicologic risks reported by a contracted pharmacologist/toxicologist were available for inspection. A summary report for the calculation of these values was available for review with validated HPLC based cleaning methods used for all cleaning validation and verification studies.

5. Complaints

Procedure for handling product complaints was available for review.

6. Product recalls

Product recall was not reviewed as all site activities were suspended in 2019.

7. Contract production, analysis and other activities

Several quality control tests as well as the qualification of certain equipment and utilities was contracted out to third party service providers. A list of service providers contract laboratories was attached in the SMF. Out sourcing and availability of contracts were inspected.

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

Self- inspections

Self-inspections (internal audits) were conducted as per the applicable SOP. This section could not be inspected in detail as site activities were suspended in 2019 during the refurbishment of the facility.

Suppliers / Vendor audit and approval

Corporate SOP addressed vendor audits and was available for inspection with vendor approvals handled by Corporate Quality Assurance (CQA). Various vendor approvals were inspected.

9. Personnel

A Site organization chart together with a Corporate organization chart was available and considered acceptable. Responsibilities for production and QC/QA were well separated. In general, the manufacturer had an adequate number of personnel with the necessary qualifications, expertise and practical experience with the Micro Labs Corporate office supporting the site with additional skills or expertise.

Job description and responsibilities for Head of Production was reviewed. Staff underwent medical checks annually. Corresponding SOP and records were available for review.

10. Training

Procedures and records were available to address and record training, together with an annual training plan which was available for all staff. Extensive training programmes were offered by the site. Training records for staff were reviewed which confirmed specific job related training completed.

11. Personal hygiene

Induction training was provided for information on Personnel Hygiene as per the applicable SOP which addressed specific hygiene topics. Direct contact was avoided between the operator's hands and starting materials, primary packaging materials, in-process material and finished products. Smoking, eating and drinking were not permitted in production, laboratory and storage areas. The level of hygiene observed, and the measures taken to maintain good practices were considered adequate. Changing rooms were provided with photos describing the gowning procedures.

12. Premises

The newly refurbished building and facilities consisted of approximately 3000 square meters of manufacturing and warehousing space plus an additional 600 square meters for Quality Control Laboratories. The facilities were located, designed, and constructed to facilitate proper cleaning, maintenance and production operations.

Production area

Production areas were walled with stainless plates to ensure surfaces were smooth and free from cracks The design of the primary and secondary manufacturing areas and work in process storage areas supported the unit processes performed and were suitably laid out to provide for a unidirectional flow of materials and to minimize the risks of cross contamination and product mix ups. The primary manufacturing areas were fitted with modern closed loop manufacturing equipment of a through-the-wall design which facilitated containment of product at source and facilitated effective cleaning. A dedicated Rifampicin dispensing cubicle was provided for the transfer of the API to the blending room immediately as required.

The primary manufacturing areas were controlled in terms of temperature and humidity by a combination of pass through and recirculating HVAC units with terminally mounted HEPA filters on the supply side (high level) and low-level exhaust. Temperature and humidity readings as well as pressure differentials were manually recorded with the installation of an automated environmental monitoring system been commenced. All logbooks reviewed were completed correctly and confirmed that the conditions were within specification.

The sampling booths and dispensing booths had separate man and material air locks and were fitted with high velocity downflow booths. Processing rooms for dust generating processes were fitted with separate man and material air locks and change rooms while the non-dust generating rooms and primary packaging rooms opened directly onto the adjacent corridors with appropriate pressure differentials. All pressure readings were within specification.

Temperature mapping

All the stores including the manufacturing area were monitored for temperature and humidity with the temperature and humidity mapping of the warehouse completed to confirm the positioning of the routine monitoring probes. During the inspection a spot check of data logger for calibration was verified and found compliant. The results of the mapping and the routine monitoring were all within specification.

Utilities

HVAC

As part of the facility upgrade, new AHU's were commissioned and validated to service the new manufacturing areas. They were all housed in a common technical area and were in a good condition with visible evidence of calibration tags and damper position indicators. The qualification documents for AHU servicing blending and granulation respectively were accurately completed and in line with expectations..

Water

A new purified water (BP) system was installed as part of the facility upgrade. Raw water was procured from a qualified external service provider and delivered to the site in tankers. Quality measures to ensure an appropriate water quality for pharmaceutical use was acceptable.

Electricity

Electricity was supplied by the local government while diesel generators supplied sufficient (excess) power to run the facility in case of power interruptions. The facility was further supported by steam generators/boilers and 2 compressed air generators.

13. Equipment

Equipment was appropriately status labelled. Balances and other measuring equipment were available for production and control activities. Where applicable, calibration due-date labels were attached to equipment. Equipment cleaning and maintenance procedures were in place.

Manufacturing Equipment

The facility was equipped with new fully integrated granulation lines of different capacities consisting of vacuum transfer systems, rapid mixer granulator, wet mill, fluidized bed drier and sifter/dry mill combinations housed in two granulation suites. The major equipment was of a through-the-wall design which reduced activities in the suite and facilitated effective cleaning. The capacity of the granulators was appropriate with the remaining equipment sized accordingly. Available was a tablet coater and compression machines with sufficient space for expansion. Strip packaging machines were housed in dedicated primary packaging cubicles linked to manual secondary packaging lines fitted with the required check weighing and over printing equipment.

Planned preventative maintenance and calibration
The Planned Preventative maintenance plan available and inspected.

14. Materials

The SOP for "Receipt, Storage, Handling and Dispatch of Finished Goods" was reviewed, challenged and found acceptable. Incoming materials were quarantined and stored in a large area that permitted batch segregation and stock rotation.

Starting Material was sampled by designated samplers. Appropriate sample sizes were calculated as per a designated sample plan supported by an SOP which addressed specific actions when defects were identified. Sampled containers were appropriated labeled.

Material was dispatched together with multi use temperature data loggers as per SOP. Software for reading results were shared with customer.

Products returned from the market are considered as per SOP.

15. Documentation

Procedures for document management were in place. Most SOPs and other documents reviewed during the inspection appeared appropriately approved by the responsible persons. Documents were regularly reviewed and kept up to date.

The batch numbering procedure. BMRs were retained for each batch processed. A new product Code was allocated for each product to be manufactured on site following the upgrade. Batch numbering was described in SOP.

16. Good practices in production

The production areas were not in operation during the audit and only the room and system logbooks together with the batch manufacturing records for the small-scale exhibit batches could be reviewed for compliance to GMP. In process testing was performed on standalone equipment which will be linked to a network-based system prior to the manufacturing of validation and commercial batches on the larger scale equipment. Compression machine punches were securely stored and cleaned in a dedicated room with adequate record keeping.

All documents reviewed were accurately completed with the attachment of the required supportive data eg labels and equipment print outs. Fixed equipment was cleaned as part of the room cleaning activities while the movable and small parts were cleaned in a cleaning area with separate clean and dirty entry points as well as storage areas for product dedicated change parts. Washing and drying facilities were provided for FBD "finger bags" along with product specific storage cabinets. Cleaning labels containing the "expiry" of the cleaning status were attached to polybags containing the cleaned parts which were then affixed to the BMR for subsequent verification.

17.Good practices in quality control

Good practices in quality control – Chemical Laboratory

The following laboratory systems were evaluated and found to be compliant.

- Receipt and storage of samples
- Preparation of analytical works sheets (AWS)
- Training and qualification of analysts
- Allocation of samples to qualified analysts
- Storage of reference samples, columns, and reagents
- Verification of analytical balances
- Standardization of volumetric solutions and analytical standards
- Data integrity of Empower 3 and selected systems
- Access and privileges for Empower 3 and Lab Solutions software
- Control of audit trails, re integration and aborted runs in Empower 3
- Review of analytical raw data
- Good chromatographic practices
- Performance and record keeping of dissolution testing
- Accuracy, review and authorization of the paper based COA generated from the AWS
- Condition and record keeping of the stability chambers
- Retention sample storage and record keeping

Micro Laboratory

The microbiology laboratory was separate from the QC laboratory with separate access to staff and dress code for staff handling sterile material. The laboratory appeared to be well equipped. Procedures and records were available for activities executed in the laboratory.

Comments:

Following the decision made to upgrade the facility, the site was partially demolished and reconstructed. During the inspection, the Inspection Team noted the comprehensive physical upgrade to the plant together with the partial upgrade in the pharmaceutical systems that supports the Pharmaceutical Quality System and GMP. Further, the site had manufactured a number of exhibit batches and intends to submit the data to the WHO seeking authorization for a manufacturing process change.

Part 3	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, the site ***Micro Labs (Kumbalgodu) – ML08, located at Micro Labs Ltd,*** located at ***15/A, 2nd Phase, Kumbalgodu Industrial Area, Bangalore 560 060, India*** complies with WHO good manufacturing practices for pharmaceutical products guidelines for the manufacture of medicines.

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.

DEFINITIONS

Critical deficiency
A *critical* deficiency may be defined as an observation that has produced, or may result in a significant risk of producing, a product that is harmful to the user.

Major deficiency
A *major* deficiency may be defined as a non-critical observation that:

- has produced or may produce a product that does not comply with its marketing authorization and/or prequalification application (including variations);
- indicates a major deviation from the GMP guide;
- indicates a failure to carry out satisfactory procedures for release of batches;
- indicates a failure of the person responsible for quality assurance/quality control to fulfil his or her duties;
- consists of several other deficiencies, none of which on its own may be major, but which together may represent a major deficiency and should be explained and reported as such.

Other deficiency
A deficiency may be classified as other if it cannot be classified as either critical or major, but indicates a departure from GMP. A deficiency may be other either because it is judged as minor or because there is insufficient information to classify it as major or critical.

Classification of a deficiency is based on the assessed risk level and may vary depending on the nature of the products manufactured, e.g. in some circumstances an example of an other deficiency may be categorized as major.

Part 4	**List of GMP Guidelines used for assessing compliance**

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
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

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
   http://www.who.int/medicines/publications/44threport/en/

3. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-sixth Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2
   Short name: WHO TRS No. 970, Annex 2
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/

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
   http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

5. WHO guidelines on good manufacturing practices for heating, ventilation and air-conditioning systems for non-sterile pharmaceutical dosage forms. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 5
   Short name: WHO TRS No. 961, Annex 5
   http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

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
   http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf?ua=1

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
   http://www.who.int/medicines/publications/44threport/en/

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 2
   Short name: WHO TRS No. 957, Annex 2
   http://www.who.int/medicines/publications/44threport/en/

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
   http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

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
    http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

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
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

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
http://whqlibdoc.who.int/trs/WHO_TRS_943_eng.pdf?ua=1

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
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

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
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

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
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

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. WHO Guidelines on good manufacturing practices: validation, Appendix 7: non-sterile process validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 3
Short name: WHO TRS No. 992, Annex 3
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.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
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

20. WHO Recommendations for quality requirements when plant – derived artemisin is used as a starting material in the prosecution 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
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

21. WHO good manufacturing practices for biological products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 3
Short name: WHO TRS No. 996, Annex 3
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex03.pdf

22. Guidance on good data and record management practices. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5
Short name: WHO TRS No. 996, Annex 5
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf

23. 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

24. WHO good manufacturing practices for biological products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 3
Short name: WHO TRS No. 996, Annex 3
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex03.pdf