

Prequalification Unit Inspection services
WHO PUBLIC INSPECTION REPORT
Finished Product Manufacturer
Remote Real Time Inspection

Part 1	General information
Manufacturers details	
Name of manufacturer	Lupin Limited
Corporate address of manufacturer	Kalpataru Inspire, 3 rd floor, off. Western express highway, Santacruz (East), Mumbai-400 055 India Tel no. (91-22) 66402323
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Lupin (Chikalthana) Lupin Ltd, A-28/1 MIDC Industrial Area, Chikalthana, Aurangabad, 431 210, India GPS coordinates: North latitude: 19°52'27.7"N East longitude: 75°22'44.9"E D-U-N-S: 862272739
Unit / block / workshop number	Blocks 1, 2 and 3
Manufacturing license number	LICENSE No: 28-499 and 25-/633 for manufacturing and marketing of pharmaceutical drug products
Dates of inspection	24, 25 and 27, 28 January 2022
Type of inspection	<i>Remote Real Time Inspection</i>
Introduction	
Brief description of the manufacturing activities	Manufacture, quality control and release of Solid Oral Dosage Forms: tablets, capsules and powders for oral suspension
General information about the company and site	Lupin Limited has its headquarters in Mumbai, India, Lupin Limited is a pharmaceutical company producing a wide range of generic and branded formulations and APIs for the developed and developing markets of the world. Lupin Limited is multidivisional and multi locational organization. The company was founded in 1968 and is currently engaged in the manufacturing of Formulations, API and Biotechnology based products. Lupin has its R & D Facilities, Lupin Research Park (LRP) at Pune and Aurangabad. Lupin has bulk drug manufacturing (API) facilities at: <ul style="list-style-type: none"> • Ankleshwar (Gujarat) • Baroda (Gujarat), • Mandideep (Madhya Pradesh) • Indore (Madhya Pradesh) • Tarapur (Maharashtra)

	<ul style="list-style-type: none"> • Vizag (Andhra Pradesh) <p>Lupin has formulation facilities at:</p> <ul style="list-style-type: none"> • Aurangabad (Maharashtra) • Indore (Madhya Pradesh) • Jammu (Jammu & Kashmir) • Mandideep (Madhya Pradesh) • Nagpur (Maharashtra) • Pune (Maharashtra) • Sikkim (Sikkim) • Verna (Goa) 																																										
History	<p>This was 3rd PQT inspection.</p> <p>The site has been inspected by the following authorities (last 5 years):</p> <table border="1"> <thead> <tr> <th>Authority</th> <th>Date/s of inspection</th> <th>Facility/block/unit covered by inspection</th> </tr> </thead> <tbody> <tr> <td>WHO (Desktop Assessment)</td> <td>16/06/2020 to 07/07/2020</td> <td>Facility</td> </tr> <tr> <td>USFDA</td> <td>10/02/2020 to 14/02/2020</td> <td>Facility</td> </tr> <tr> <td>CDSCO, FDA, India</td> <td>03/10/2019 to 04/10/2019</td> <td>Facility</td> </tr> <tr> <td>USFDA</td> <td>06/05/2019 to 15/05/2019</td> <td>Facility</td> </tr> <tr> <td>National Drug Authority, UGANDA</td> <td>20/09/2018 to 21/09/2018</td> <td>Facility</td> </tr> <tr> <td>Hungary</td> <td>25/03/2019</td> <td>Facility</td> </tr> <tr> <td>MoH, Kenya</td> <td>21/02/2018 to 22/02/2018</td> <td>Facility</td> </tr> <tr> <td>MoH, YEMEN</td> <td>15/01/2018</td> <td>Oral Liquid Facility</td> </tr> <tr> <td>WHO Geneva, Switzerland</td> <td>07/11/2017 to 10/11/2017</td> <td>Facility</td> </tr> <tr> <td>CDSCO, FDA, India</td> <td>31/07/2017 to 01/08/2017</td> <td>Facility</td> </tr> <tr> <td>USFDA</td> <td>24/07/2017 to 28/07/2017</td> <td>Facility</td> </tr> <tr> <td>USFDA</td> <td>17/04/2017 to 26/04/2017</td> <td>Oral Liquid Facility</td> </tr> <tr> <td>TFDA, Taiwan</td> <td>14/03/2017 to 17/03/2017</td> <td>Block 1</td> </tr> </tbody> </table>	Authority	Date/s of inspection	Facility/block/unit covered by inspection	WHO (Desktop Assessment)	16/06/2020 to 07/07/2020	Facility	USFDA	10/02/2020 to 14/02/2020	Facility	CDSCO, FDA, India	03/10/2019 to 04/10/2019	Facility	USFDA	06/05/2019 to 15/05/2019	Facility	National Drug Authority, UGANDA	20/09/2018 to 21/09/2018	Facility	Hungary	25/03/2019	Facility	MoH, Kenya	21/02/2018 to 22/02/2018	Facility	MoH, YEMEN	15/01/2018	Oral Liquid Facility	WHO Geneva, Switzerland	07/11/2017 to 10/11/2017	Facility	CDSCO, FDA, India	31/07/2017 to 01/08/2017	Facility	USFDA	24/07/2017 to 28/07/2017	Facility	USFDA	17/04/2017 to 26/04/2017	Oral Liquid Facility	TFDA, Taiwan	14/03/2017 to 17/03/2017	Block 1
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Brief report of inspection activities undertaken – Scope and limitations																																											
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Restrictions	N/A																																										
Out of scope	Products out of scope of WHO PQ																																										
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Abbreviations	Meaning
ADE	Acceptable daily exposure
ADR	Adverse drug reaction
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APQR	Annual product quality review
AQL	Acceptance quality limit
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CCEA	Complete, consistent, enduring, available
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
CD	Compact disk
CV	Curriculum vitae
DQ	Design qualification
DVD	Digital versatile disk
EDI	Electronic deionization
EHS	Environment, health, safety
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GC	Gas chromatography (or gas chromatography equipment)
GMP	Good manufacturing practices
GPT	Growth promotion test
GxP	Good “variable” practices The variable “x” depends on the application of the standards. The “x” can be C for “Clinical”, D for ‘Distribution’, L” for Laboratory” or M for ‘Manufacturing’
GQCSC	Global quality council steering committee
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high-performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IC	Ion chromatography (or ion chromatography equipment)
IQ	Installation qualification
LAF	Laminar air flow
LCL	Lower control limit
LIMS	Laboratory information management system

LoD	Loss in drying
MACO	Maximum allowable carryover
MB	Microbiology
MBL	Microbiology laboratory
MET	Microbial enumeration test
MF	Master formulae
MR	Management review
NC	Non-conformity
NCA	National control authority
NCL	National control laboratory
NRA	National regulatory agency
OOC	Out of calibration
OOS	Out of specification
OQ	Operational qualification
OOT	Out of trend
NMT	Not more than
PDE	Permitted daily exposure
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
QAMS	Quality assurance management system
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
RPN	Risk priority number
SQCM	Site Quality Council Meeting
SMF	Site master file
SOP	Standard operating procedure
UCL	Upper control limit
UHPLC	Ultra-high-performance liquid chromatography (or ultra-high-performance liquid chromatography equipment)
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer
WFI	Water for injection

Part 2	Summary of the findings and comments
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NOTE:

CORPORATE AND SITE-SPECIFIC SOPS WERE SUBMITTED WELL BEFORE INSPECTION DATES AND CHECKED BY INSPECTORS IN ADVANCE

Inspection was focused on general Quality Management System and procedures

1. Quality system

Principle

Production and control operations were specified in written form and GMP requirements were essentially being met. Managerial responsibilities were specified in written job descriptions. Product and processes were monitored, and the results were checked as part of the approval process for batch release. Regular monitoring and reviews of the quality of pharmaceutical products were being conducted according to documented schedules and procedures.

Quality Assurance Management System (QAMS) is an electronic system and was used for the initiation, execution, review and approval of quality management documents, for example deviations, CAPAs, etc.

Data integrity policy

Data integrity policy was in place. Corporate SOP “Data Governance” was checked. SOP defined the main components of a data governance intended to ensure the accuracy, consistency, and completeness of data throughout its lifecycle when such data is generated to support the product quality, safety, and efficacy. The scope of the SOP covered operational activities that have direct impact on the integrity of data. SOP was applicable to all Lupin sites that are manufacturing and distributing healthcare products for human consumption and to all data generated manually or electronically

Electronic data

The following corporate SOPs were available and checked:

- SOP “Back up, Restoration and Archival of Computerized system”
- SOP “Disaster Management & Business Continuity Plan for Computer Software System”
- SOP “Standalone Computer Software System Administration”

The following site-specific SOPs were available and checked:

- SOP “User Management and Periodic Review of Audit Trail”
- SOP “Assigning Users/System Policies and Management of Electronic Data in Chromeleon Network”
- SOP “User management of Electronic Data in Standalone Software”

Isoniazid/Rifampicin Tablets 75mg/150mg, batch XX test Assay (HPLC) sequence audit trail, injection audit trail, system audit trail, method audit trial was presented and checked.

Product Quality Review (PQR)

Corporate SOP “Annuals Product Quality Review of drug products” was checked. According to the SOP all commercialized products was subjected to annual review including products where no batches were manufactured during the review period as well as synopsis of scale-up / exhibit batches (if executed) of the product which were analyzed.

Statistical evaluation to determine the maximum, minimum, mean was carried out for batch yield, relevant in process and finished product test parameters. Process capability index (CpK) value was calculated for batch yield and key quantitative analytical results like Assay and Related Substances.

The following APQRs were checked:

- TB068 Isoniazid/Rifampicin Tablets 75mg/150mg review period Feb 2020 – Jan 2021
- TB070 Ethambutol hydrochloride/ Isoniazid/ Pyrazinamide/Rifampicin Tablets 275mg /75mg /400mg /150mg, review period Mar 2020 – Feb 2021

Management review (MR)

Corporate SOP “Management review of Quality Metrics” was checked. Management review was performed monthly.

Complaints

Corporate “Handling of Market Complaints for drug products” and complaints register for 2021 were checked. Site QA and Quality Assurance or Contract Manufacturing QA were responsible for complaints investigation.

Complaints were categorized:

- Category I: Critical
- Category II: Major
- Category III: Minor
- Category IV: Adverse Drug Event (ADE)

A number of complaint files were checked.

Recalls

Corporate SOP “Recall/Market Withdrawal of Drug Products” and List of market withdrawal 2021 was checked.

Recalls were voluntary and statutory and were classified as:

- Class I
- Class II
- Class III

There were three recall levels specified:

- Consumer or user level
- Retail level
- Wholesale level

Two recall files were checked:

Rejection/returns

SOP “Handling of Recalled/Returned Goods” and rejected batch register 2021 and SOP “Handling of Data Loggers” were checked.

Quality Risk Management

Corporate SOP “Quality Risk Management” and Quality Risk Management (QRM) Protocol/report Rifabutin capsules USP 150 mg were checked. SOP provided the principles and examples of tools for quality risk management that was applied to different aspects of pharmaceutical quality.

Change control

Corporate SOP “Change control” and lists of permanent CC, temporary CC and CC for WHO products were checked. SOP was applicable to changes related to Manufacturing Facilities, Procurement, Warehousing, Distribution, Equipment, Utilities, Manufacturing Processes, Materials/Products, systems and instruments, document management systems such as Specifications, Test Methods and Operating Procedures. Quality Unit was responsible for the oversight of the change control system.

Trends for 2021 were checked. A number of change controls were checked.:

Deviation management

Corporate SOP “Handling of deviations” and deviations register for WHO products were checked. Deviations were classified as:

- Critical
- Major
- Minor

A Quality Risk Assessment was required for all major and critical deviations and as needed for minor deviations.

Deviation trends were prepared and evaluated quarterly by QA within 30 days of the quarter end to determine if there were any trends developing which could be indicative of systemic problems.

A number of deviation records and related CAPAs were checked.

Trends October 2021 – December 2021 were checked.

Corrective and preventive actions (CAPAs)

Corporate SOP “Corrective Action and Preventive action” and register for 2021 were checked. The SOP was applicable, but not limited to:

- Product Complaint
- Product Failure
- OOS Result
- Recalls/Return
- Deviation
- Audit
- Rejection
- Management Review
- OOT Result
- Regulatory Inspection Finding
- Trends from process performance and product quality monitoring
- OOC Result
- Laboratory incident
- Annual Product Review Report
- Improvements in design of Quality system

Self-inspection

SOP “Self-Inspection”, self-inspection planners QA/QC August 2021, self-inspection check-lists QA/QC August 2021, self-inspection reports QA/QC for August 2021, self-inspection compliance reports QA/QC August 2021 and periodic review of self-inspection QA/QC August 2021 were checked.

Supplier approval

Corporate SOP “Vendor Qualification” was checked. SOP was applicable for suppliers of the following materials:

- Active pharmaceutical ingredients
- Excipients
- Empty capsules
- Intermediates and API-SM (KSM)
- Other than KSM (Raw material)
- Primary packaging materials
- Secondary packaging materials
- Tertiary packaging materials Device Constituent part
- Devices
- Gases
- Solvents
- Solvents used in formulation

On-site audits and approval of vendors was carried out by corporate QA. Approved suppliers list was managed by SAP system. Vendor disapproval procedure was explained.

Technical agreement with API manufacturer and audit report were checked. Contract giver and acceptor responsibilities were specified.

Contract testing

SOP “Qualification of Contract Testing Laboratories” was checked. According to the SMF no contract manufacturing was carried out.

16 contract testing laboratories were used.:

Technical agreement with contract laboratory and compliance report were checked.

Documentation

SOP_AUR_QA_009530 (4.0) “Document Control” was checked.

Batch Numbering

Corporate SOP “Assignment of Batch Number, Manufacturing Date and Retest/Expiry Date” was checked. Batch numbers were automatically generated during process order creation in SAP system. In case one semi-finished batch was packed into multiple different packs; each different pack was assigned a unique batch number.

Batch release

SOP “Batch Release System” and batch release register 2021 and SOP “Part Release of Batch” were checked.

BMR/BPR

Corporate SOP “Preparation, Review and Approval of Batch Manufacturing and Batch Packaging Records” was checked.

BMR for Rifampin and Isoniazid Tablets (150 mg/75 mg), batch No XX and BPR for Rifampin and Isoniazid Tablets (150 mg/75 mg), batch No YY and Analytical Record for batch No. VV were checked.

Personnel

Corporate SOP “Training of Personnel” was checked. SOP was applicable to initial and ongoing technical training of new and existing employees at manufacturing and research sites of Lupin Limited. It covers both permanent and contractual staff. It is also applicable to the corporate employees who are involved in GxP activities. The following types of training programs were specified:

Corporate SOP “Analyst Qualification” was checked. According to the SOP Analyst qualification is a process to evaluate proficiency of the analyst to satisfactorily perform analysis using specific analytical technique with desired precision.

Corporate SOP “Microbiologist Qualification” was checked. According to the SOP, the Microbiologist Qualification is a process to evaluate proficiency of the microbiologist to satisfactorily perform analysis using specific microbiological technique with desired precision.

Personnel according to the SMF:

Department	No of employees
Production	216
Engineering/safety/purchase	19
Global supply chain organization	4
QA/QC	155
Stores/distribution/excise	38
Process Development Laboratory	11
Regulatory Affairs	3
Accounts	2
Administration	2
Operational Excellence	1
Infotech	5
HR	3
Total	459

Personnel Hygiene

SOP “Health and Hygiene” was checked.

2. Production system

A virtual tour of the site was conducted, which included both Block 1, Block 2 and Block 3.

The following areas were covered:

- Warehouse
- Manufacturing
- Utilities (Purified Water system and HVAC)

Process validation

Corporate SOP “Process Validation for Drug Products” was checked.

Process validation protocol and report for product Ethambutol HCL and Isoniazid Tablets (400mg/150 mg) was checked.

Hold time studies

Corporate SOP “Hold Time Studies for Drug Products” was checked.

A number of hold time studies were checked.

SOP “Procedure for correction of wrong entry in document” was checked.

Cleaning validation

Corporate SOP “Cleaning Validation for Drug Products” and Cleaning Validation Master Planner for Block 1 was checked.

3. Facilities and equipment system

Equipment qualification/maintenance

The following SOPs were checked:

- Corporate SOP “Qualification Procedure for Analytical Instrument & Equipment”
- Corporate SOP “Qualification of Equipment. System and Facility for manufacturing/Packaging of Drug Products
- Corporate SOP “Validation of Computerized Software System”
- SOP “Calibration of Measuring Instruments”

(already mentioned as second bullet)

A number of equipment qualifications were checked.

Utilities

HVAC

SOP “Environmental Monitoring (EM) of Oral Solid Dosage Formulation Facility” and EM trends checked. Action and alert limits were specified.

EM trend data of production Block 2 for period May - August 2021 was checked.

Purified water (PW)

PW trends 1st December – 31st December 2021 for return loop (blocks 1, 2 and 3) were checked. Action and alert limits were specified.

4. Laboratory control system

Laboratory premises

A virtual tour of the laboratories was conducted, which included both the Chemistry and Microbiology laboratories.

OOS investigation records:

Corporate SOP “Handling of Out of Specification Test Results”, and OOS registers chemistry and microbiology were checked. Phase I and Phase II investigations were applied. In the event an OOS result is confirmed, and an assignable root cause is identified during investigation, the risk assessment impact was performed on other manufactured batches.

Site specific SOP “Handling and Investigation of Out of Specification Microbiological Tests” was checked.

A number of OOS and OOS trends October 2021 – December 2021 were checked.

Out of Trends (OOT)

Corporate SOP “Trend Analysis of Quality Parameters and Out of Trend Investigation”, OOT register 2021 and trends were checked.

Laboratory investigations

Corporate SOP “Handling of Laboratory Incidents” was checked.

A number of incident files and trends were checked.

Chromatography

Corporate SOP “Good Chromatographic Practices and Documentation” was checked. SOP was applicable for good chromatographic practices and documentation of chromatographic data.

Reference materials

Corporate SOP “Procurement, Storage, Qualification and Handling of Analytical Standards” was checked.

The in-house reference standard was dispensed / filled (approx. 50 to 200 mg) with appropriate safety precautions or preferably under laminar airflow in small amber colored glass bottles or vials and then stoppered/crimped.

Retention samples

Corporate SOP “Retention Sample management” was checked. According to the SOP, retention samples were stored in their marketable packs or in the simulated market pack or more protective packaging than the marketed packaging system. The samples were stored in a secured area with limited access. Retention samples were stored for one-year after expiry or as per country specific regulatory agency guideline, whichever is the greater.

Site specific SOP “Handling, Recording and Cleaning of Retention/Control Sample area” and SOP “HPLC/GC Column Management” were checked.

Analytical test sheets

SOP “Preparation, Review, Issuance and Control of Test Data Sheet” was checked. SOP was applicable for preparation, merging, uploading, review, approval/ blocking, linking, issuance and revision of e-test data sheet (e-TDS) for recording of analytical raw data through SAP.

Isoniazid/Rifampicin Tablets 75mg/150mg, batch XX analytical raw data sheets were checked. Audit trail for Isoniazid 100mg Tablets identity test by stand-alone IR was checked.

Microbiology laboratory

The following SOPs were checked:

- SOP “Good Microbiology Practices”
- SOP “Preparation/Disposal of Microbial Culture Media”
- SOP “Procedure for Handling of Ready to Use Lyophilized Form (Bioball™) of Microbial Strains”

The following records were checked:

- Media Preparation Record, Growth Promotion Test Report and Sterilization Cycle Report
- Microbiological Test Data Sheet for TAMC/TYMC/E. coli by pour plate of Rifampin, Isoniazid, Pyrazinamide and Ethambutol HCL Tablets

The following calibration was checked:

- Calibration report for Autopipette

The following validations/equipment qualifications were checked:

- Periodic Re-Validation protocol and report of LAF units and Bio-safety cabinet
- Validation protocol and report for HPHV steam Sterilizer
- Validation protocol and report of Temperature Mapping of Incubators

5. Materials system

The following documents were checked:

- Corporate SOP “Transportation study of Drugs Products”
- SOP “Receipt and Storage of packaging Materials in Warehouse”
- SOP “Receipt and Storage of Raw Materials in Warehouse”
- SOP “Sampling, Testing, Release and Rejection of Raw Materials”. Raman spectrophotometer was used for 100 % identity tests, in case Raman spectrophotometer was not implemented, samples were collected from individual containers.
- SOP Sampling and Visual Inspection of Packaging Material”. Sampling was carried in accordance to AQL. Defects were specified
- SOP “Dispensing of Packaging Materials and Labels”
- SOP “Temperature/ RH Mapping in Materials/product Storage Area”
- SOP “Handling of Dataloggers”

6. Packaging and labelling system

The following documents were checked:

- SOP “Receipt/Issue, Storage and Control of Packaging Materials and Packaging Operation”
- SOP “Functioning of the Packaging Department”

Part 3	Initial conclusion – Inspection outcome
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Based on the areas inspected, the people met and the documents checked, and considering the findings of the inspection, including the observations listed in the Inspection Report *Lupin Ltd (Chikalthana) Blocks 1, 2 and 3, located at A-28/1 MIDC Industrial Area, Chikalthana, Aurangabad, 431 210, India* was considered to be operating at an acceptable level of compliance with WHO good manufacturing practices for pharmaceutical products 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.

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 to be 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 referenced in the inspection report
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1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-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 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
4. 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

5. 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
6. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1. **Short name: WHO TRS No. 957, Annex 1**
<http://www.who.int/medicines/publications/44threport/en/>
7. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3. **Short name: WHO TRS No. 957, Annex 3**
<http://www.who.int/medicines/publications/44threport/en/>
8. 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
9. 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
10. Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9. **Short name: WHO TRS No. 961, Annex 9**
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1
11. 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
12. 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
13. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2. **Short name: WHO TRS No. 981, Annex 2**
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

14. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3. **Short name: WHO TRS No. 981, Annex 3**
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/
15. 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_w eb.pdf
16. 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_w eb.pdf
17. 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_w eb.pdf
18. 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 Multisource guidance or WHO TRS No. 996, Annex 10**
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf
19. 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**
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_1010/en/
20. 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
21. 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>

22. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4. **Short name: WHO TRS No. 1025, Annex 4**
<https://www.who.int/publications-detail/978-92-4-000182-4>
23. Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 6. **Short name: WHO TRS No. 1025, Annex 6**
<https://www.who.int/publications-detail/978-92-4-000182-4>
24. Points to consider when including Health-Based Exposure Limits (HBELs) 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 1033, Annex 2**
<https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations>
25. 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 1033, Annex 3**
<https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations>
26. 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 1033, Annex 4**
<https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations>