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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Desk Assessment of Finished Pharmaceutical Product (FPP) Manufacturer

Part 1	**General information**
Company information	
Name of Manufacturer	Lupin Limited
Corporate address of manufacturer	Kalpatru Inspire, 3rd Floor, Off Western Express Highway, Santacruz (East) Mumbai 400 055, Maharashtra, India
Inspected site	
Name & address of manufacturing site	Lupin Limited A-28/1 MIDC Industrial Area, Chikalthana, Jalna Road, Aurangabad 431 210, Maharashtra, India
Production Block/Unit	Not applicable
Desk assessment details	
Date of review	07 July 2020
Products covered by this desk assessment	1. Rifabutin Capsules150mg (HA640) 2. Isoniazid/Rifampicin Film-coated Tablet, 75mg/150mg (TB068) 3. Ethambutol/Isoniazid/Pyrazinamide/Rifampicin Film-coated Tablet 275mg/75mg/400mg/150mg (TB070) 4. Ethambutol hydrochloride Film-coated Tablet, 400mg (TB177) 5. Isoniazid/Rifampicin Dispersible Tablet, 30mg/60mg (TB184) 6. Isoniazid/Pyrazinamide/Rifampicin Dispersible Tablet, 30mg/150mg/60mg (TB185) 7. Isoniazid/Rifampicin Tablet, 150mg/150mg (TB195) 8. Isoniazid Tablet, 100mg (TB196) 9. Ethambutol hydrochloride/Isoniazid Film-coated Tablet, 400mg/150mg (TB198) 10. Ethambutol hydrochloride/Isoniazid/Rifampicin Film-coated Tablet, 275mg/75mg/150mg (TB199) 11. Protionamide Film-coated Tablet, 250mg (TB206) 12. Ethionamide Tablet, 250mg (TB207)

Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
USFDA	Dates of inspection:	10-14 February 2020
	Type of inspection:	General cGMP and post-approval inspection
	Block/Unit:	Not indicated
	Type of products/Dosage forms covered:	Finished dosage form
USFDA	Dates of inspection:	6-15 May 2019
	Type of inspection:	General cGMP inspection
	Block/Unit:	Not indicated
	Type of products/Dosage forms covered:	Finished dosage form
USFDA	Dates of inspection:	24-28 July 2017
	Type of inspection:	Pre-approval (PAI) inspection.
	Block/Unit:	Not indicated
	Type of products/Dosage forms covered:	Oral liquid and Capsule facility
USFDA	Dates of inspection:	17-26 April 2017
	Type of inspection:	cGMP and preapproval inspection
	Block/Unit:	Not indicated
	Type of products/Dosage forms covered:	Oral suspension, tablets, capsules and liquid (focus on Atovaquone oral suspension)
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	7-10 November 2017, Compliant	
Brief description of manufacturing activities	The facility at Aurangabad was engaged in manufacturing of oral solid dosage forms, liquids, nasal solutions and powders for oral suspension.	
General information about the company and manufacturing site	The company was established in 1968 and its headquarters were located in Mumbai. It had 18 manufacturing facilities globally, including 5 API sites and 8 FPP sites in India. The Aurangabad facilities started their operations in 1978 and were located approximately 2 Km from Aurangabad airport. There were 3 manufacturing blocks on site. WHO prequalification products were manufactured in all 3 blocks. An extension to Block 1 was introduced in 2016.	
Focus of the last WHO inspection	Routine GMP inspection	

Areas inspected	**Document reviewed including but not limited** • Organization Chart • Job descriptions for key personnel • Personnel training and hygiene • Product Quality Review • Quality Risk Management • Responsibilities of the quality units and production • Complaints and Recalls • Deviation control and change control • CAPA procedure • OOS and investigation • Material release • Self-inspection and vendor qualification • Validation and qualification • Equipment calibration • Data integrity • Sampling and testing of materials • Batch processing records • Materials management system • Purified water system **Site visited:** • Starting material warehouse • OSD Production operations (Blocks 1, 2, 3) • QC laboratories including chemical and microbiological • Controlled samples and Documentation area • Stability chambers area
Out of scope and restrictions (last WHO inspection)	Products not submitted to WHO for Prequalification. The focus of the inspection included storage, production quality control areas where WHO prequalification products were manufactured.
WHO products covered by the last WHO inspection	HA640 Rifabutin Capsules, hard 150mg TB068 Isoniazid/Rifampicin Tablet, Film-coated 75mg/150mg TB070 Ethambutol hydrochloride/Isoniazid/Pyrazinamide/Rifampicin Tablet, Film-coated 275mg/75mg/400mg/150mg TB177 Ethambutol hydrochloride Tablet, Film-coated 400mg TB184 Isoniazid/Rifampicin Tablet, Dispersible 30mg/60mg TB185 Isoniazid/Pyrazinamide/Rifampicin Tablet, Dispersible 30mg/150mg/60mg TB195 Isoniazid/Rifampicin Tablet 150mg/150mg TB196 Isoniazid Tablet 100mg TB198 Ethambutol hydrochloride/Isoniazid Tablet, Film-coated 400mg/150mg TB199 Ethambutol hydrochloride/Isoniazid/Rifampicin Tablet, Film-coated 275mg/75mg/150mg TB206 Protionamide Tablet, Film-coated 250mg TB207 Ethionamide Tablet 250mg

Additional products covered by this desk assessment:	None

Abbreviations	**Meaning**
AHU	Air handling unit
API	Active pharmaceutical ingredient
BMR	Batch manufacturing record
BPR	Batch production record
CAPA	Corrective and preventive action
CC	Change control
GMP	Good manufacturing practices
NC	Non conformity
NRA	National regulatory agency
PQR	Product quality review
PQS	Pharmaceutical quality system
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
SOP	Standard operating procedure

Part 4	**Summary of the assessment of supporting documentation**

a) Manufacturing authorization and GMP certificate granted by the local authority:

The Manufacture License (25-633 and 28-499) is renewed on 2 August 2016 and it is valid up to 1 August 2021. The certificate of GMP (WHO-GMP/CERT/AD/89420/2019/11/29673) was issued by the State FDA of Maharashtra, India. The certificate was renewed, and it is valid until 3 April 2023.

b) Site master file (SMF):

The site master file (SMF/AUR/09 effective date 28/02/2020) of the manufacturing facility was provided. In general, the SMF provided a high-level overview of the manufacturing facility located in Chikalthana, Aurangabad.

c) List of regulatory inspections performed in the last 3 years and their outcome:

Sr. No.	Date of Audit	Name and country of competent authority	Outcome
1.	14/03/2017 to 17/03/2017	TFDA, Taiwan	Audit closed and Approval received
2.	17/04/2017 to 26/04/2017	USFDA, USA	Audit closed and EIR received
3.	24/07/2017 to 28/07/2017	USFDA, USA	Audit closed and EIR received
4.	31/07/2017 to 01/08/2017	CDSCO, FDA, India	Audit closed and Approval received
5.	07/11/2017 to 10/11/2017	WHO Geneva, Switzerland	Audit closed and Approval received
6.	15/01/2018	MoH, Yemen	Audit closed and Approval received
7.	21/02/2018 to 22/02/2018	MoH, Kenya	Audit closed and Approval received
8.	20/09/2018 to 21/09/2018	National Drug Authority, Uganda	Audit closed and Approval received
9.	06/05/2019 to 15/05/2019	USFDA	Audit closed and EIR received
10.	03/10/2019 to 04/10/2019	CDSCO, FDA, India	Audit closed and Approval received
11.	10/02/2020 to 14/02/2020	USFDA	Audit closed and EIR received

d) List of all the products and dosage forms manufactured on-site:

The list of all products (total 101) and dosage forms manufactured at the Chikalthana site was provided. The site produces tablets, capsules, oral suspension, syrup, and solution/drops. From the information provided, it was noted that the site is a multi-product or shared facility which produces different dosage forms and products of different therapeutic categories.

e) Most recent product quality review(s) (PQR)(s) of the concerned WHO product(s):

The PQRs of the following products were provided and reviewed:

1. HA640 Rifabutin capsules 150mg (Feb 2019-Jan 2020): One batch was produced during the review period whereas a total of 3 batches was released. The PQR included the review of critical process parameters, critical quality attributes, batch yield and analytical data. The process capability index was not part of the review as less than 10 batches were produced during the review period. There were no out of specification, out of trend, deviation and rejection reported during the review period. A total of 58 change controls (54 Minor, 4 Major whereas 37 closed and 21 still open), were initiated. No market complaint, adverse events, recalls, field alert reporting were reported during this period. In general, the PQR of Rifabutin capsules 150mg was conducted adequately.

2. TB068 Rifampin 150mg and Isoniazid 75mg tablets (Feb 2019-Jan 2020): A total of 308 batches were manufactured during this review period whereas 305 released, two (2) under review and one (1) rejected. The PQR included the review of critical process parameters, critical quality attributes, batch yield and analytical data. CpK values for dissolution, assay, related substances and batch yield of product Rifampin and Isoniazid Tablets calculated and CpK values for batch yield, all quality attributes except isoniazid assay found more than 1.33. The CpK for Isoniazid assay was reported 1.16 against 1.33 and an assessment was carried out to find out the root cause of low CpK. The assay values for certain batches were in the range of 95.4% and 104.2% against the specification limit of 95.0-105.0% which resulted to lower CpK. There was no root cause identified, hence no CAPA implemented. The PQR reported 2 valid OOS, 7 OOT, 3 deviations, 1 rejection (Batch No A903181 due to low assay content of Isoniazid) during the review period. A total of 81 change controls (64 closed and 17 still open) were initiated during the review period. There was no market complaint, adverse event, recall and returns observed and reported. In general, the PQR of Rifampin 150mg and Isoniazid 75mg tablets was conducted adequately.

3. TB070 Rifampin 150mg, Isoniazid 75mg, Pyrazinamide 400mg and Ethambutol Hydrochloride 275mg tablets (Mar 2019-Feb 2020): A total of 385 batches were manufactured (363 released, 7 rejected, 12 under investigation and 3 under analysis) during this review period. The PQR included the review of critical process parameters, critical quality attributes, batch yield and analytical data. Process capability index of dissolution, assay, related substances and batch yield for batches of product Rifampin, Isoniazid, Pyrazinamide and Ethambutol HCL tablets USP manufactured and analyzed in this review period were calculated. CpK values for batch yield, all quality attributes (Dissolution, related substances, Assay) except Rifampin assay and Ethambutol HCL assay found more than 1.33. This indicates process was capable of a normally distributed population. CpK value for Rifampin assay and Ethambutol HCL assay found less than 1.33 i.e. 1.24 and 1.31 respectively. The PQR reported 2 OOS, 17 OOT, no deviation, no market complaint, no adverse event, no recall, no return and 7 batches rejected. A total of 74 change controls (69 Minor and 5 Major whereas 63 closed and 11 still open) were initiated. In general, the PQR of TB070 was conducted adequately.

4. TB177 Ethambutol Tablets 400mg (Apr 2018-Mar 2019): A total of 78 batches (under two product codes) were manufactured (18 to be packed). The PQR included the review of critical process parameters, critical quality attributes, batch yield and analytical data. Process capability index (CpK) of the assay, dissolution, residual solvents and batch yield for batches of product Ethambutol tablets BP 400 mg manufactured and analysed in this review period were calculated. There was no OOS, OOT, deviation, market complaint, adverse event, recall, returns and batch rejection reported during the review period. There were 4 valid OOS and 9 OOT reported for stability study during the review period. A total of 48 change controls (45 Minor and 3 Major whereas 39 closed and 9 still open) were initiated during the review period. In general, the PQR of TB177 was conducted adequately.

5. TB184 Rifampicin 60mg and Isoniazid 30mg dispersible tablets (Akurit Kid, Feb 2019-Jan 2020): One (1) batch was manufactured and released during the review period. The PQR included the review of critical process parameters, critical quality attributes, batch yield and analytical data. As less than 10 batches manufactured, process capability index for analytical parameters and batch yield was not calculated. There were no OOS, OOT, deviation, batch rejection, market complaint, adverse event, recall and returns reported during the review period. A total of 49 change controls (44 Minor and 5 Major whereas 35 closed and 14 still open) were initiated during the review period. In general, the PQR of TB184 was conducted adequately.

6. TB185 Rifampicin 60mg, Isoniazid 30mg and Pyrazinamide 150mg tablets (Akurit Z Kid Tablets, Feb 2019- Jan 2020): During the review period of no batch was manufactured and released. A total of 48 change controls (46 Minor and 2 Major whereas 37 closed and 11 still open). There were two recalls reported for TB185 during the review period. In general, the PQR of TB185 was conducted adequately.

7. TB195 Rifampin 150mg and Isoniazid 150mg tablets (Jan-Dec 2019): A total of five (5) batches were manufactured (4 released and 1 rejected). There was no OOS, deviation, complaint, adverse event, recall reported during the review period. One batch was rejected due to OOT for the stability study. A total of 61 change controls (56 Minor and 5 Major whereas 49 closed and 12 still open) were initiated. Although a sufficient number of batches were not produced during the review period, it was noted that CpK for dissolution and related substances was above 1.33 whereas CpK for Isoniazid/Rifampcin assay and batch yield was below 1.33. In general, the PQR of TB195 was conducted adequately.

8. TB196 Isoniazid 100mg tablets (Apr 2018-Mar 2019): A total of thirteen (13) batches were manufactured and released during the review period. The PQR included the review of critical process parameters, critical quality attributes, batch yield and analytical data. Process capability index (CpK) of assay, dissolution, related substances and batch yield for batches of product Isoniazid Tablets BP 100 MG manufactured and analysed in this review period were calculated. CpK values of dissolution, assay and related substances were observed more than 1.33, however, batch yield were observed less than 1.33. Further assessment was done to identify the cause of variability for batch yield. There was no OOS, one OOT, one deviation, no batch rejection, no market complaint, no adverse event, no recall and no return reported during the review period. A total of 45 change controls (42 Minor, 3 Major whereas 39 closed and 6 still open). In general, the PQR of TB196 was conducted adequately.

9. TB198 Ethambutol HCl 400mg and Isoniazid 150mg tablets (May 2018 – Apr 2019): No batch was manufactured and released during the review period. A total of 33 change controls (29 Minor, 4 Major whereas 25 closed and 8 still open) were initiated during the review period. The batches put up for stability study were reviewed and trended, one valid OOS was reported for the stability study. In general, the PQR of TB198 was conducted adequately.

10. TB199 Rifampin 150mg, Isoniazid 75mg and Ethambutol HCl 275mg tablets (Feb 2019-Jan 2020): A total of nine (9) batches were manufactured and released during the review period. The PQR included the review of critical process parameters, critical quality attributes, batch yield and analytical data. The CpK for dissolution, the assay, related substances and batch yield of product was calculated and noted that all quality attributes except isoniazid and ethambutol assay found more than 1.33. The CpK value for Isoniazid assay was found 1.32 and for Ethambutol assay found 1.03. The further assessment was done for the same to identify the cause of variability. There was no OOS, OOT, deviation, batch rejection, adverse event, recall and return reported except one complaint. A total of 58 change controls (52 Minor, 6 Major whereas 48 closed and 10 still open) were initiated during this period. In general, the PQR of TB199 was conducted adequately.

11. TB206 Prothionamide tablets 250mg (May 2018-Apr 2019): A total of 5 batches (two different product codes) were manufactured and released during the review period. The PQR included the review of critical process parameters, critical quality attributes, batch yield and analytical data. There was no OOS, OOT, deviation, batch rejection, market complaint, adverse event, recall, return reported during the review period. A total of 48 change controls (44 Minor, 4 Major whereas 34 closed and 14 still opened) were initiated. In general, the PQR of TB206 was conducted adequately.

12. TB207 Ethionamide 250mg tablets (May 2018- April 2019): A total of two (2) batches manufactured (one released during the review period). The PQR included the review of critical process parameters, critical quality attributes, batch yield and analytical data. CpK value of analytical parameters and for batch yield was not calculated in this review period as batches manufactured in current and previous review period were less than 10. There was no OOS, deviation, batch rejection, complaint, adverse event, recall and return reported during the review period. A total of 42 change controls (40 Minor, 2 Major whereas 30 closed and 12 still open) were initiated during the review period. In general, the PQR of TB207 was conducted adequately

f) Batch manufacturing and packaging record(s), including the analytical part, for the most recently released batch of relevant product(s):

The batch manufacturing, packaging records and test data sheet for the following products were provided by the manufacturer.

1. HA640 Rifabutin Capsules 150mg (the batch record A808954)
2. TB068 Isoniazid/Rifampicin Film-coated Tablet, 75mg/150mg (the batch record A000334, A000848,)
3. TB070 Ethambutol/Isoniazid/Pyrazinamide/Rifampicin Film-coated Tablet 275mg/75mg/400mg/150mg (the batch record A000514 and A000515)
4. TB177 Ethambutol hydrochloride 400 mg (the batch record A903417 and A806460)
5. TB184 Isoniazid/Rifampicin Dispersible Tablet, 30mg/60mg **(product withdrawn)**
6. TB185 Isoniazid/Pyrazinamide/Rifampicin Dispersible Tablet, 30mg/150mg/60mg **(product withdrawn)**
7. TB195 Isoniazid/Rifampicin Tablet, 150mg/150mg (the batch record A804874)
8. TB196 Isoniazid Tablet, 100mg (the batch record A000089)
9. TB198 Ethambutol hydrochloride/Isoniazid Film-coated Tablet, 400mg/150mg
10. TB199 Ethambutol hydrochloride/Isoniazid/Rifampicin Film-coated Tablet, 275mg/75mg/150mg (the batch record A801377 and A802238)
11. TB206 Prothionamide Film-coated Tablet, 250mg (the batch record A905254)
12. TB207 Ethionamide Tablet, 250mg (the batch record A901994)

In general, the submitted batch manufacturing, packaging and test data sheets (HPLC chromatograms for assay, related substance and residual solvents, where applicable not provided) appeared adequate.

g) Master batch manufacturing and packaging record(s) of the product(s) of interest:

The Master batch manufacturing and packaging records for the following products are provided:

1. HA640 Rifabutin Capsules 150mg
2. TB068 Isoniazid/Rifampicin Film-coated Tablet, 75mg/150mg
3. TB070 Ethambutol/Isoniazid/Pyrazinamide/Rifampicin Film-coated Tablet 275mg / 75mg / 400mg /150mg
4. TB177 Ethambutol hydrochloride 400 mg
5. TB195 Isoniazid/Rifampicin Tablet, 150mg/150mg
6. TB196 Isoniazid Tablet, 100mg
7. TB199 Ethambutol hydrochloride/Isoniazid/Rifampicin Film-coated Tablet, 275mg/75mg/150mg
8. TB206 Prothionamide Film-coated Tablet, 250mg
9. TB207 Ethionamide Tablet, 250mg

No master manufacturing and packaging record was provided for the following products:

1. TB184 Isoniazid/Rifampicin Dispersible Tablet, 30mg/60mg
2. TB185 Isoniazid/Pyrazinamide/Rifampicin Dispersible Tablet, 30mg/150mg/60mg
3. TB198 Ethambutol hydrochloride/Isoniazid Film-coated Tablet, 400mg/150mg

In general, the submitted master manufacturing and packaging records appeared adequate.

h) Recalls in the past three years related to products with quality defects:

The manufacturer has provided a list of recalls for products during 2017, 2018, 2019 and 2020. It was noted that a total of 16 recalls (15 related to TB products and 1 Valsartan) were initiated between 2017 and 2020 and these were classified as Class III (except Pyzina 1000, Valsartan classified as Class II). The TB products were primarily recalled due to out of specification observed for dissolution, water content, related substance and assay tests at various stability study timepoints.

i) Confirmation by the senior quality assurance representative that a full self-inspection or external audit dedicated to the product(s) has been performed and all matters dealt with:

The manufacturer has confirmed that self-inspections are conducted at least twice in a year as per the defined schedule. In addition, the site is also audited by its corporate quality team at least once per year.

j) copy of any warning letter, or equivalent regulatory action, issued by any authority to which the site provides or has applied to provide the product:

The manufacturer has confirmed that no warning letter or equivalent regulatory action, issued to Lupin Chikalthana, Aurangabad site by any authority.

k) Out-of-stock situations:

The manufacturer has confirmed that there is no out of stock situation arise until now.

l) Additional documents submitted:

The manufacturer has confirmed that they have not received any notification from the competent regulatory authorities for the next 6 months.

In addition, the manufacturer has provided details of the manufacturing process for the Prequalified products covered by the inspection of the competent regulatory authorities. It was confirmed that various manufacturing rooms/facilities where WHO PQ products are manufactured, covered by the competent regulatory authorities.

Part 5	Conclusion – Desk assessment 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 ***Lupin Limited A-28/1, MIDC, Industrial Area, Chikalthana, Jalna Road, Aurangabad 431 210, India*** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

This WHOPIR will remain valid until June 2022, provided that the outcome of any inspection conducted during this period is positive.

Part 6	List of guidelines referenced in this 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 GMP Guidelines*** or ***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 GMP for APIs*** or ***WHO TRS No. 957, Annex 2***
   http://apps.who.int/medicinedocs/documents/s20119en/s20119en.pdf

3. WHO guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report. Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 9. ***Short name: WHO TRS 1010, Annex 9***
   https://www.who.int/medicines/areas/quality_safety/quality_assurance/TRS1010annex9.pdf?ua=1

4. 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/

5. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4.
   Short name: WHO TRS No. 929, Annex 4
   http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

6. 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 HVAC Guidelines*** *or* ***WHO TRS No. 1010, Annex 8***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_1010/en/

7. 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

8. 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 GPPQCL guidelines **or** ***WHO TRS No. 957), Annex 1***
   http://www.who.int/medicines/publications/44threport/en/

9. 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/

10. 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

11. 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

12. 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

13. 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

14. 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

15. 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/

16. 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/

17. 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

18. 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

19. 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

20. WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5. ***Short name: WHO TRS No. 992, Annex 5***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

21. 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 GDRMP guidelines or ***WHO TRS No. 996, Annex 5***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf

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