World Health Organization

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

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

Part 1	**General information**	
Company information		
Name of Manufacturer	Sandoz Private Limited	
Corporate address of manufacturer	Kalwe MIDC, Plot No. 8-A/2, 8-B,T.T.C. Industrial Area, Kalwe Block, Village-Dighe, Opp. Thane-Belapur Road, Navi Mumbai 400 708, India	
Inspected site		
Name & address of manufacturing site	Kalwe MIDC, Plot No. 8-A/2, 8-B,T.T.C. Industrial Area, Kalwe Block, Village-Dighe, Opp. Thane-Belapur Road, Navi Mumbai 400 708, India	
Production Block	MDT TB, FDF plant	
Desk assessment details		
Date of review	08 to 12 June 2020	
Products covered by this desk assessment	TB 85 Rimactazid (Isoniazid/ Rifampicin)75mg/150mg TB 90 Rimstar 4 FDC (Ethambutol hydrochloride /Isoniazid/Pyrazinamide /Rifampicin, Film coated) 275/75/400/150mg TB379 Clofazimine Capsules, soft 50mg (Secondary packing, testing and release) TB 380 Clofazimine Capsules, soft 100mg (Secondary packing, testing and release)	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
USA FDA	Dates of inspection:	4 to 12 April 2019
	Type of inspection:	Preannounced cGMP inspection
	Block/Unit:	FDF plant (MDT TB was not covered)
	Type of products/Dosage forms covered:	OSDs including tablets and capsules

AGES Austria	Dates of inspection:	25 – 27 February 2020
	Type of inspection:	Preannounced GMP inspection
	Block/Unit:	FDF plant (MDT TB was covered)
	Type of products/Dosage forms covered:	The inspection concentrated on the manufacture and control of the following products: •Tacrolimus HGC 0,5mg, 0,75mg, 1mg, 2mg, 5mg •Allopurinol TAB 100mg, 300mg
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	14 - 17 February 2011 GMP compliance	
Brief description of manufacturing activities	Production, quality control and product release of oral solid dosage forms (i.e. tablets & capsule)	
General information about the company and manufacturing site	Sandoz Private Limited Kalwe is specialized in the manufacturing of solid oral solid dosage forms including tablets & capsules. This site has increased its manufacturing capacity and expanded for manufacturing of Multi Drug Therapy (MDT) – TB products.	
Focus of the last WHO inspection	The inspection covered various sections of the WHO GMP text, including premises, equipment, documentation, materials, validation, sanitation and hygiene, production, quality control and utilities.	
Areas inspected	MDT TB production block was visited. Documents reviewed included (but not limited to): • Batch records • Deviations • Change control • Complaints • Recalls • Various SOPs • Calibration and qualification procedures and records • Preventive maintenance (PM) procedures, schedules and records • Stability testing • Validation Master Plan • Process validation protocols/reports	
Out of scope and restrictions (last WHO inspection)	FPP's testing laboratory was not inspected. APIs testing laboratory was not inspected in detail.	

WHO products covered by the last WHO inspection	TB085 Rifampicin/Isoniazid 150/75mg coated tablet TB090 Rifampicin/Isoniazid/Pyrazinamide/Ethambutol hydrochloride 150/75/400/275mg film coated tablet
Additional products covered by this desk assessment:	TB379 Clofazimine Capsules, soft 50mg (2nd packing, testing & release) TB380 Clofazimine Capsules, soft 100mg (2nd packing, testing & release)
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:
Provided, reviewed and considered acceptable.

b) Site master file:
Provided, reviewed and considered acceptable.

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

The site was inspected by the following authorities during the review period:

Sr. No.	Name of Inspectorate	Inspection Dates	Scope
1.	Competent Authority of Austria (AGES, EU)	25th -- 27th Feb 2020	GMP Inspection
2.	Indian Health Authority (CDSCO)	13th - 14th Jan 2020	GMP Inspection (Renewal of WHO - GMP Certificate)
3.	National Drug Authority, Uganda	29th - 30th Aug 2019	GMP Inspection
4.	USFDA, USA.	4th - 12th Apr 2019	GMP Inspection
5.	Indonesia Health Authority	30th Oct - 1st Nov 2018	GMP Inspection
6.	Saudi Arabia Health Authority	07th - 8th May 2018	GMP Inspection
7.	ANVISA (Brazil)	2nd - 5th Apr 2018	GMP Inspection
8.	Indian Health Authority (CDSCO)	24th - 25th May 2017	GMP Inspection (Renewal of WHO - GMP Certificate)
9.	Tunisia Health Authority	8th - 10th May 2017	GMP Inspection
10.	Nigeria Health Authority (NAFDAC)	28th Apr 2017	GMP Inspection
11.	Russia Health Authority	20th – 21st Apr 2017	GMP Inspection
12.	Turkey Health Authority	10th - 14th Apr 2017	GMP Inspection
13.	USFDA	23rd Feb - 3rd Mar 2017	GMP Inspection
14.	Competent Authority of Austria (AGES, EU)	10th - 13th Jan 2017	GMP Inspection
15.	Taiwan BFDA	24th - 27th Oct 2016	GMP Inspection
16.	Belarus Health Authority	05th - 6th Oct. 2016	GMP inspection
17.	National Drug Authority, Uganda	21st - 22nd Mar. 2016	GMP Inspection
18.	Zimbabwe Health Authority	23rd - 24th Feb 2015	GMP inspection

d) List of all the products and dosage forms manufactured on-site:
List of dosage forms manufactured including the common name (where available) for the active pharmaceutical ingredients (API) used was provide.

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

1. Product: Lamprene Capsules 50mg and 100mg (TB 379 and TB380)
Review Period: 01 April 2018 to 31 March 2019
Summary: Lamprene Capsules are packed in two strengths 50 mg and 100 mg at Sandoz Private Limited, Kalwe for France and WHO scopes. Only packing is done at Sandoz Private Limited, Kalwe. The capsules are procured from a German company.
No stability failure was reported for product storage condition. Based on the available data the shelf life and storage condition designed for the product has been maintained. No batch was rejected during the review period.

2. Product: Rimstar Film Coated Tablets (TB90 4FDC)
Review Period: 01 December 2018 to 30 November 2019
Summary: Commercial batches of Rimstar FCT were manufactured and packed for EU market during the review period. No stability failure was reported. No batch rejected during the review period.

3. Product: Rimactazid 150mg / 75mg Film Coated Tablets (TB85 2FDC)
Review Period: 01 September 2018 to 31 August 2019
Summary: A batch of Rimactazid 150mg/75mg FCT was manufactured during the review period. No stability failure was reported. No batch rejected during the review period.

f) Batch manufacturing and packaging record(s), including the analytical part, for the most recently released batch of relevant product(s):
BMR, BPR and testing records of the product in scope were provided, reviewed with no objectional findings.

g) Process validation and master batch manufacturing and packaging record(s) of the product(s) of interest:
Provided, reviewed and no objectional findings.

h) Recalls in the past three years related to products with quality defects:
Product recall list provided. 6 recall occurred during period May 2017 - May 2020.

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:
Self-inspection SOP and schedule provided, reviewed and no objectional findings.

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:
No warning letter or equivalent regulatory action had been issued for the site during past three years.

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 ***Sandoz Private Limited*** located at ***Kalwe MIDC, Plot No. 8-A/2, 8-B,T.T.C. Industrial Area, Kalwe Block, Village-Dighe, Opp. Thane-Belapur Road, Navi Mumbai 400 708, India*** is operating at an acceptable level of compliance with WHO GMP guidelines.

This compliance status shall be valid until ***31 December 2022*** or when another inspection is conducted by WHO or by a stringent regulatory authority.

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 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. 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/

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

21. 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

22. 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

23. 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

24. 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

25. 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

26. 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