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WHO Prequalification Unit – Inspection Services
WHO INSPECTION REPORT
(WHOPIR)
Desk Assessment of Finished Product Manufacturer

Part 1	**General information**
Company information	
Name of Manufacturer	Cipla Ltd
Corporate address of manufacturer	Cipla House Peninsula Business Park Ganpatrao Kadam Marg Lower Parel, Mumbai-400 013 India
Inspected site	
Name & address of manufacturing site	Cipla Ltd. Unit III Plot No. L-139 to L-146, Verna Industrial Estate, Verna, Salcette, Goa. Pin: 403 722, India
Production Block/Unit	Unit III
Manufacturing license number	536 in Form 25 valid up to 18/10/2026
Desk assessment details	
Start and end dates of review	28 April - 1 May 2025
Products covered by this desk assessment	1. Lamivudine/Zidovudine Tablet, Film-coated 150mg/300mg 2. Efavirenz/ Emtricitabine/ Tenofovir disoproxil fumarate Tablet, Film coated 600mg/200mg/300mg
List of documents submitted	a. Regulatory Inspections List (last 3 years) b. Current full inspection report (Past 3 years) c. Proof of CAPA implementation-Latest inspection report d. Manufacturing Authorization and GMP certificate e. Site Master File f. List of all the products and dosage forms manufactured on-site g. Product Quality Reviews h. Completed BMR and BPR including the analytical part i. List of Recalls (Past 3 years) j. A confirmation by Self-inspection or external audit k. Master BMR and BPR-WHO products l. Copy of any warning letter, or equivalent regulatory action

	m.Description of recent or foreseen out-of-stock situations n. A list of upcoming inspections (next 6 months) o. Manufacturing Process for the concerned products covered by the inspection of the competent SRA authorities performed (Past 3 years)	
Any documents missing?	None.	
Part 2	**Summary of SRA/NRA inspection evidence considered and comments**	
US FDA, USA	Dates of inspection:	10 to 21 June, 2024
	Type of inspection:	Un-announced for-cause GMP inspection
	Block/Unit:	Unit I, Unit III, Unit IV, Unit V, Unit VII, Unit VIII and Unit X.
	Type of products/Dosage forms covered:	Sterile and non-sterile drug products for the US market including oral solid dosage, topical gel/cream, sterile inhalation products and sterile injectable products.
Landesamt for Soziales, Jugend und Versorgung (LSJV), Germany (on behalf of EMA)	Dates of inspection:	06 to 09 November, 2023
	Type of inspection:	Routine product related GMP Inspection
	Block/Unit:	Unit III, Unit IV and Microbiology Lab in Unit II
	Type of products/Dosage forms covered:	Oral solid dosage: Tablets
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	18-20 and 22-23 March 2019 GMP compliant after CAPAs.	
Brief summary of manufacturing activities	Unit III: Production and quality control of • Semi-solid dosage forms: Topical Preparations • Solid Dosage Forms: Uncoated, Coated tablets	
General information about the company and manufacturing site	Cipla Ltd. is a public limited company established in 1935. It manufactures a wide range of pharmaceutical formulations, Active Pharmaceutical Ingredients & Medical device products. The site at Goa including 9 Units (in operation) are engaged in manufacturing of pharmaceutical formulations. Each manufacturing unit has independent water system, warehouse, technical floor for HVAC systems and Analytical Laboratory.	

Focus of the last WHO inspection	The focus of the inspection included storage, production and quality control areas where WHO Prequalification products were manufactured.
Areas inspected	**Document reviewed including but not limited** • Organization Chart • Job descriptions for key personnel • Product Quality Review • Quality Risk Management • Management Review • Responsibilities of the quality units and production • Complaints and Recalls • Deviation control and change control • OOS and investigation • CAPA procedure • Material release • Validation and qualification • Equipment calibration • Data integrity • Sampling and testing of materials • Batch processing records • Materials management system • Purified water system **Sites visited** Unit III- stores, production and packing
Out of scope and restrictions (last WHO inspection)	Products not submitted to WHO for Prequalification was out of inspection scope.

WHO products covered by the last WHO inspection

	WHO No.	Product Name	Manufacturing Unit	
List of products commercially supplied since last WHO inspection in June 2016				
1.	HA039	Nevirapine Tablet 200mg	III & (IV, VII)	
2.	HA060	Lamivudine/Zidovudine 150/300mg tablets	III & VII (IV)	
3.	HA365	Lamivudine/ Nevirapine/ Zidovudine 150/200/300mg tablets	III & VII (IV)	
4.	HA352	Efavirenz Tablet, Film coated 600mg	IV & VII	
5.	HA439	Emtricitabine/ Tenofovir disoproxil fumarate 200/300mg fil coated tablet	VII & (III, IV)	
6.	HA500	Efavirenz/ Emtricitabine/ Tenofovir	VII & (III, IV)	

		disoproxil fumarate 600/200/300 film coated tablet		
7.	HA401	Tenofovir disoproxil fumarate 300mg film coated tablet	VII & (III, IV)	
8.	HA593	Efavirenz/ Lamivudine/ Tenofovir 600/300/300mg tablets	VII & VII PDII	
9.	RH039	Misoprostol tablet 200mcg	VIII	
10.	RH040	Levonorgestrel Tablet 750mcg	VIII	
11.	RH046	Levonorgestrel Tablet 1.5mg	VIII	
13.	HA353	Lamivudine Tablet 150mg	III, IV & VII	
14.	MA064	Artemether/ Lumefantrine tablets 20/120mg	III, IV & VII	
15.	TB205	Levofloxacin Tablet Film coated 250mg	III, IV & VII	
16.	TB227	Levofloxacin Tablet Film coated 500mg	III, IV & VII	
17.	HA352	Efavirenz Tablet Film coated 600mg	III	
18.	TB228	Cycloserine Capsules 250mg	IV & VII	
19.	HA518	Abacavir and Lamivudine 60/30mg	VII	
20.	IN013	Oseltamivir PO4 Capsules hard 45mg	VII	
21.	IN012	Oseltamivir PO4 Capsules hard 30mg	VII	
22.	IN001	Oseltamivir PO4 Capsules hard 75mg	VII	
23.	RH030	Ethinylestradiol/ Levonorgestrel + Placebo Ethinylestradiol/ Levonorgestrel Tablet + Placebo tablet 0.03mg/0.150mg+0mg	VIII	

Dossier under assessment

HA702	Dolutegravir/ Lamivudine/ Tenofovir disoproxil fumarate 50 mg/ 300 mg/ 300 mg Tablets	VII & VII PD II

Additional products to be 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
FPP	Finished pharmaceutical product
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
SMF	Site master file
SOP	Standard operating procedure

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

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

Sr. No	Regulatory Authority	Date of Inspection	Compliance Action Status
1.	US FDA	10-21 June 2024	VAI
2.	MCAZ, Zimbabwe	2-3 April 2024	Approved
3.	LSJV, Germany (on behalf of EMA, Europe)	6-9 November 2023	Approved
4.	ANVISA, Brazil	28 - 31 August 2023	Approved
5.	MOH Libya	7-9 August 2023	Approved
6.	MOH Yemen	3-4 July 2023	Company Re-registration. Certificate awaited
7.	TGA, Australia	22 – 29 April 2023	Approved
8.	PPB, Kenya	03 – 04 February 2023	Approved
9.	TMDA Tanzania	16-17 November 2022	Approved
10.	CDSCO & DFDA, Goa Joint Inspection	21-22 September 2022	Approved

11.	EAEU (conducted by Kazakhstan Authority)	12-15 September 2022	Approved
12.	US FDA	16-26 August 2022	OAI
13.	EDA, Egypt	17-24 August 2022	Approved

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

1. The copy of following manufacturing licenses issued by Food &Drugs Administration (FDA), Goa, India was provided.

Name of the licence holder and Address	Licence no.	Valid up to
M/s Cipla Limited, Plot No. L-139 to L-146, Verna, Salcete Goa, 403722	536 in Form 25	18/10/2026

2. The copy of GMP certificate No.721/MFG/WHO-GMP/DFDA/2022/2874 issued by Food & Drugs Administration, Government of Goa, India on 16/12/2022 was provided, which is valid until 30 November 2025.

c) Site master file:

The copy of Site Master File: SMF/CIP/GOA/F Version No.: 18, effective on 26 September 2024, copy of P & ID of Water System and copy of P & ID of Air Handling Unit were provided and reviewed with no objectional findings.

According to the SMF, 3270 people was employed on the Goa site, which included 1669 in Production, 407 in QA and 917 in QC Department, 159 in Storage and distribution and 118 in Engineering Department. No activity other than manufacturing of pharmaceutical formulations is carried out at the site. Site does not manufacture sensitizing materials like Beta-lactams (Penicillin) or Cephalosporin or biological preparations e.g., live organisms. Types of products currently manufactured on-site were documented in the SMF. The site has 9 different units and Unit IX was shut down. The following products were manufactured in Unit III.

- Semi-solid dosage forms: Topical Preparations
- Solid Dosage Forms: Uncoated, Coated tablets

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

The list of all the products and dosage forms manufactured on-site was provided and reviewed.

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

The prequalification status of products was provided by the company.
Commercial batches of Lamivudine/Zidovudine Tablet, Film-coated 150mg/300mg and Efavirenz/Emtricitabine/Tenofovir disoproxil fumarate Tablet, Film-coated 600mg/ 200mg/ 300mg have not been manufactured since 2016 and 2015 respectively. The APQRs for other markets were provided and briefly reviewed with no objectional findings.

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

The BMRs/BPRs including the analytical part of commercial batches of Lamivudine/Zidovudine Tablet, Film-coated 150mg/300mg and Efavirenz/Emtricitabine/Tenofovir disoproxil fumarate Tablet, Film-coated 600mg/ 200mg/ 300mg for other market provided were briefly reviewed with no objectional findings.

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

Master BMRs/BPRs provided were briefly reviewed with no objectional findings.

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

There are no product recalls in the last 3 years.

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 company confirmed that, as per Internal Audits SOP, the internal audits program is being carried out at a defined frequency for Goa site. The internal audits were conducted at., Unit III, IV, VII, VII PD II and VIII at Goa site of Cipla Ltd. and each reported observation was satisfactorily complied.

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 company declare that, No warning letter, or equivalent regulatory action, issued by any authority to Cipla Ltd. Unit III, Plot No. L-139 to L-146, Verna Industrial Estate, Verna, Salcette, Goa. Pin: 403 722, India.

k) Out-of-stock situations:

The company declared that, the products which were commercialized were found/observed with no out of stock situation.

l) Additional documents submitted:

The company provided the information for upcoming inspection to Cipla Ltd. Unit III by national 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 **Cipla Ltd. Unit III** located at **Plot No. L-139 to L-146, Verna Industrial Estate, Verna, Salcette, Goa, 403722, India** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

Part 6	List of GMP Guidelines referenced in the inspection report

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO TRS No. 986, Annex 2***

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***

3. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3.
   Short name: WHO TRS No. 1033, Annex 3

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

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***

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

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

8. WHO good practices for pharmaceutical products containing hazardous substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3.
   Short name: WHO TRS No. 957, Annex 3

9. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-sixth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 2.
   Short name: WHO TRS No. 1044, Annex 2

10. WHO guidelines on technology transfer in pharmaceutical manufacturing. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-sixth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
    Short name: WHO TRS No. 1044, Annex 4

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**

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***

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

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

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

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

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

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***

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***

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

21. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4. ***Short name: WHO TRS No. 1033, Annex 4***

22. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
Short name: WHO TRS No. 996, Annex 10

23. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 10.
Short name: WHO TRS No. 1010, Annex 10

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

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

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

27. Production of water for injection by means other than distillation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 3. ***Short name: WHO TRS No. 1025, Annex 3***

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

29. WHO good practices for research and development facilities of pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-sixth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 6. ***Short name: WHO TRS No. 1044, Annex 6***

30. WHO good manufacturing practices for investigational products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-sixth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 7. ***Short name: WHO TRS No. 1044, Annex 7***

31. WHO good manufacturing practices for excipients used in pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052), Annex 2. ***Short name, WHO TRS No. 1052, Annex 2***