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

WHO Prequalification Unit – Inspection Services
WHO PUBLIC 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 VIII, Plot No. S-103 to S-105, S-107 to S-112, L-147, L-147/1 to L-147/3, L-138 and L-147/A; Verna Industrial Estate, Verna, Salcette, Goa. Pin: 403 722, India
Production Block/Unit	Unit VIII
Desk assessment details	
Start and end dates of review	21-25 April 2025
Products covered by this desk assessment	1. RH046 Levonorgestrel Tablet 1.5mg 2. RH040 Levonorgestrel Tablet 750mcg 3. RH039 Misoprostol Tablet 200mcg
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 three years) j. A confirmation by SQA -Self-inspection or external audit k. Master BMR and BPR-WHO product(s) 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 six 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.
Sachsen Anhalt, Germany	Dates of inspection:	29 February, 1st March, and 4 March, 2024
	Type of inspection:	Product-related GMP inspection
	Block/Unit:	Unit VIII
	Type of products/Dosage forms covered:	Bulk medicinal product finasteride 5 mg film-coated 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 VIII: Production and quality control of hormonal tablets, hard gelatin capsules, topical preparations and liquid injectables.	
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	

<table>
<tr><td></td><td>

- 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 VIII- stores, production, packing, quality control and technical floor
</td></tr>
<tr><td>Out of scope and restrictions (last WHO inspection)</td><td>Products not submitted to WHO for Prequalification was out of inspection scope.</td></tr>
<tr><td>WHO products covered by the last WHO inspection</td><td>
<table>
<tr><th></th><th>WHO No.</th><th>Product Name</th><th>Manufacturing Unit</th></tr>
<tr><td colspan="4">List of products commercially supplied since last WHO inspection in June 2016</td></tr>
<tr><td>1.</td><td>HA039</td><td>Nevirapine Tablet 200mg</td><td>III & (IV, VII)</td></tr>
<tr><td>2.</td><td>HA060</td><td>Lamivudine/Zidovudine 150/300mg tablets</td><td>III & VII (IV)</td></tr>
<tr><td>3.</td><td>HA365</td><td>Lamivudine/ Nevirapine/ Zidovudine 150/200/300mg tablets</td><td>III & VII (IV)</td></tr>
<tr><td>4.</td><td>HA352</td><td>Efavirenz Tablet, Film coated 600mg</td><td>IV & VII</td></tr>
<tr><td>5.</td><td>HA439</td><td>Emtricitabine/ Tenofovir disoproxil fumarate 200/300mg fil coated tablet</td><td>VII & (III, IV)</td></tr>
<tr><td>6.</td><td>HA500</td><td>Efavirenz/ Emtricitabine/ Tenofovir disoproxil fumarate 600/200/300 film coated tablet</td><td>VII & (III, IV)</td></tr>
<tr><td>7.</td><td>HA401</td><td>Tenofovir disoproxil fumarate 300mg film coated tablet</td><td>VII & (III, IV)</td></tr>
<tr><td>8.</td><td>HA593</td><td>Efavirenz/ Lamivudine/ Tenofovir 600/300/300mg tablets</td><td>VII & VII PDII</td></tr>
<tr><td>9.</td><td>HA353</td><td>Lamivudine Tablet 150mg</td><td>III, IV & VII</td></tr>
<tr><td>10.</td><td>MA064</td><td>Artemether/ Lumefantrine tablets 20/120mg</td><td>III, IV & VII</td></tr>
<tr><td>11.</td><td>TB205</td><td>Levofloxacin Tablet Film coated 250mg</td><td>III, IV & VII</td></tr>
<tr><td>12.</td><td>TB227</td><td>Levofloxacin Tablet Film coated</td><td>III, IV & VII</td></tr>
</table>
</td></tr>
</table>

		500mg	
13.	HA352	Efavirenz Tablet Film coated 600mg	III
14.	TB228	Cycloserine Capsules 250mg	IV & VII
15.	HA518	Abacavir and Lamivudine 60/30mg	VII
16.	IN013	Oseltamivir PO4 Capsules hard 45mg	VII
17.	IN012	Oseltamivir PO4 Capsules hard 30mg	VII
18.	IN001	Oseltamivir PO4 Capsules hard 75mg	VII
19.	RH039	Misoprostol Tablet 200mcg	VIII
20.	RH040	Levonorgestrel Tablet 750mcg	VIII
21.	RH046	Levonorgestrel Tablet 1.5mg	VIII
22.	RH030	Ethinylestradiol/Levonorgestrel + Placebo Ethinylestradiol/ Levonorgestrel Tablet + Placebo Tablet 0.03mg/0.150mg+0mg	VIII

Dossier under assessment

HA702	Dolutegravir/Lamivudine/Tenofovir disofloxil fumarate 50mg/300mg/300mg 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	Nonconformity
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	Dates of Inspection	Regulatory Authority	Outcome
1.	10-21 June 2024	US FDA	VAI
2.	28 March 2024	MCAZ, Zimbabwe	Approved
3.	29 February, 1st March, and 4 March, 2024	Sachsen Anhalt, Germany	Approved
4.	7-9 August 2023	MOH Libya	Approved
5.	3-4 July 2023	MOH Yemen	Company Re-registration. Certificate awaited
6.	20 – 24 March 2023	INVIMA, Colombia	Approved
7.	14-15 November 2022	TMDA Tanzania	Approved
8.	16-26 August 2022	US FDA	OAI
9.	17-24 August 2022	EDA, Egypt	Approved
10.	25-26 April 2022	CDSCO and DFDA, Goa Joint Inspection	Approved
11.	Desk assessment	TGA, Australia	Approved
12.	08 July 2022 (Desk Assessment)	RFDA, Rwanda	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 license holder and Address	License no.	Valid up to
M/s Cipla Limited, Plot No. S-103 to S-105, S-107 to S-112, L-138, L-147, L-147/1 to L-147/3, L-147-A, Verna Industrial Estate, Verna, Salcete-Goa - 403 722.	611 in Form 28	18/03/2028
	616 in Form 25	19/05/2028

2. The copy of GMP certificate No. 789/MFG/WHO-GMP/DFDA/2022/886 issued by Food &Drugs Administration, Government of Goa, India on 22/06/2022 was provided, which is valid until 13th June 2025.

c) Site master file:

The copy of current version of Site Master File, 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, no activity other than manufacturing of pharmaceutical formulations is carried out at the site. The site does not manufacture sensitizing materials like Beta-lactams (Penicillin) or Cephalosporin or biological preparations e.g., live organisms.

The site has 9 different units and Unit IX was shut down. The Hormone preparations are handled in a stand-alone dedicated facility Unit VIII. Types of products currently manufactured on-site were documented in the SMF.

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. Coated, uncoated tablets, hard gelatin capsules, topical preparations, topical solutions of non-sterile hormone products are manufactured in Unit VIII.

The following product have been withdrawn after last WHO inspection:

RH030 Ethinylestradiol/ Levonorgestrel + Placebo Ethinylestradiol/ Levonorgestrel Tablet + Placebo tablet 0.03mg/0.150mg+0mg.

e) Most recent product quality reviews (PQRs) of the concerned WHO products:

The following APQRs provided by the company were reviewed with no objectional findings.

Sr. No	PQ No.	FPP	APQR
1	RH046	Levonorgestrel Tablet 1.5mg	Reporting period: NOV. 2023 TO OCT. 2024
2	RH040	Levonorgestrel Tablet 750mcg	Reporting period: JUN. 2023 TO MAY 2024
3	Rh039	Misoprostol Tablet 200mcg	Reporting period: NOV. 2023 TO OCT. 2024

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 Levonorgestrel Tablet 1.5mg and Misoprostol Tablet 200mcg provided were briefly reviewed with no objectional findings.

Levonorgestrel Tablet 750mcg has not been released to WHO as well as for any other country as per WHO manufacturing formula and process since June 2019. No documents were provided. The BMRs/BPRS will be verified in next inspection.

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.

Master BMRs/BPRS of Levonorgestrel Tablet 750mcg prequalified will be verified in next inspection as no batches released since June 2019 and the company will perform a new process validation.

h) Recalls in the past three years related to products with quality defects:
A recall list was provided and reviewed. No recall of WHO PQed products reported in past three 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, currently, no warning letter, or equivalent regulatory action, is in force by any authority to Cipla Ltd. Unit VIII, Plot No. S-103 to S-105, S-107 to S-112, L-147, L-147/1 to L-147/3, L-138 and L-147/A; Verna Industrial Estate, Verna, Salcette, Goa. Pin: 403 722, India.

k) Out-of-stock situations:
The company declared that “No out-of-stock situation recorded/foreseen."

l) Additional documents submitted:
The company provided the information for upcoming inspection to Cipla Ltd. VIII 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 VIII** located at **Plot No. S-103 to S-105, S-107 to S-112, L-147, L-147/1 to L-147/3, L-138 and L-147/A; Verna Industrial Estate, Verna, Salcette, Goa, 403 722, 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***