World Health Organization

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**Prequalification Unit Inspection services**
**WHO PUBLIC INSPECTION REPORT**

**Desk Assessment of Finished Product Manufacturer**

| **Part 1** | **General information** |
|---|---|
| **Company information** | |
| Name of Manufacturer | Micro Labs Limited |
| Corporate address of manufacturer | Micro Labs Limited<br>31 Racecourse Rd<br>Bengaluru 560 001<br>India |
| **Inspected site** | |
| Name & address of manufacturing site | Micro Labs Limited<br>Unit 3<br>92 SIPCOT Industrial complex<br>Hosur<br>Tamil Nadu<br>635 126<br>India |
| Production Block/Unit | Unit-3 (ML03) |
| **Desk assessment details** | |
| Date of review | 23 December 2022 |
| Products covered by this desk assessment | |

| PQT Number | Finished Pharmaceutical Product | Prequalification status |
|---|---|---|
| TBD | Artemether/Lumefantrine Tablet 20mg/120mg | Under Assessment |
| TBD | Artemether/Lumefantrine Tablet, Dispersible 20mg/120mg | Under Assessment |
| TB348 | Isoniazid Tablet, Dispersible 100mg | Prequalified |
| TB356 | Levofloxacin Tablet, Dispersible 100mg | Prequalified |
| TB237 | Levofloxacin Tablet, Film-coated 250mg | Prequalified |
| TB238 | Levofloxacin Tablet, Film-coated 500mg | Prequalified |
| TB239 | Protionamide Tablet, Film-coated 250mg | Prequalified |
| TB242 | Ethionamide Tablet, Film-coated 250mg | Prequalified |
| TB323 | Linezolid Tablet, Film-coated 600mg | Prequalified |
| TB368 | Ethambutol hydrochloride Tablet, Dispersible 100mg | Prequalified |
| TBD | Linezolid Tablet, Dispersible 150mg | Under Assessment |
| TB355 | Levofloxacin Tablet, Film-coated 750mg | Prequalified |
| TB263 | Moxifloxacin (hydrochloride) Tablet, Film-coated 400mg | Prequalified |

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|---|---|---|---|
| | TB352 | Ethionamide Tablet, Dispersible 125mg | Prequalified |
| | TB335 | Pyrazinamide Tablet, Dispersible 150mg | Prequalified |
| | TB367 | Ethambutol hydrochloride Tablet, Dispersible 50mg | Prequalified |
| | TB349 | Moxifloxacin (hydrochloride) Tablet, Dispersible 100mg | Prequalified |
| | TB347 | Isoniazid Tablet, Dispersible 50mg | Prequalified |
| | TB171 | Pyrazinamide Tablet 400mg | Prequalified |
| | TB172 | Pyrazinamide Tablet 500mg | Prequalified |
| | TB173 | Isoniazid Tablet 100mg | Prequalified |
| | TB174 | Isoniazid Tablet 300mg | Prequalified |
| | TB331 | Ethionamide Tablet, Film-coated 125mg | Prequalified |

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| List of documents submitted | See below | |
| Any documents missing? | No | |
| **Part 2** | **Summary of SRA/NRA inspection evidence considered (from most recent to last) and comments** | |
| *UK MHRA* | Dates of inspection: | 28 July 2020 |
| | Type of inspection: | Remote assessment |
| | Block/Unit: | Unit-3 |
| | Type of products/Dosage forms covered: | Oral Solid Dosage forms. (Non-sterile tablets and capsules) |
| | Physical areas inspected: | Documentation review of facility expansion for supply of products to the UK market<br><br>Report covered elements of QMS, personnel, premises and equipment, documentation, production activities, |
| | Final conclusion of the inspection report: | Acceptable |
| **Part 3** | **Summary of the last WHO inspection** | |
| Date and conclusion of most recent WHO inspection | 8 to 10 April 2019<br><br>Compliant | |
| Summary of manufacturing activities | Production of tablets and capsules | |

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|---|---|
| General information about the company and manufacturing site | Micro Labs Limited is engaged in the manufacture of medicinal products since 1973 for domestic and export markets. Company was engaged in the manufacture of various therapeutic segments including cardiovascular, psychotropic, neurological, anti-diabetic, gynecological, gastro-enterological, dermatological and ophthalmic products. The company has a total of 14 manufacturing facilities for the manufacture of products for domestic and export markets.<br><br>Micro Labs Hosur site has three Units, location I & II and Unit-3. This manufacturing facility (Unit-3) also includes a small scale manufacturing area for producing scale-up batches, bio-batches and products which require small batch sizes for commercial requirements. The equipment in this area is of similar type and operating principle as that of equipment used for manufacture of commercial scale batches. This manufacturing facility was commissioned in the year 2003. |
| Focus of the last WHO inspection | Special inspection to review CAPA relating to the control of cross-contamination, and review cleaning validation approach while considering HBEL. |
| Areas inspected | Special inspection to review CAPA relating to the control of cross-contamination, and review cleaning validation approach while considering HBEL. |
| Out of scope and restrictions (last WHO inspection) | None |
| WHO products covered by the last WHO inspection | See scope: Special inspection to review CAPA relating to the control of cross-contamination, and review cleaning validation approach while considering HBEL. |
| Additional products to be covered by this desk assessment: | See list in this report |
| **Abbreviations** | **Meaning** (Delete abbreviations that do not apply to your type of report or add additional ones if needed) |
| 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** |
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**a) List of all regulatory inspections performed in the last 5 years and their outcomes:**

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|---|---|---|
| September 2018. | TGA Australia | Compliant |
| November 2018, | UK MHRA | Compliant |
| April 2019, | UK MHRA, WHO PQ, Unicef | Compliant |
| July 2020, | UK MHRA, desk assessment | Compliant |

**b) Manufacturing authorization granted by national authorities:**

Issued by Department of Food Safety and Drugs Control Administration
Tamil Nadu
India
TN00003934
TN00003935

**c) Site master file:**

SMF ML03:024 was submitted and generally acceptable.
Filters indicated in schematic drawings for the HVAC system were referenced by international classification.

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

See attached

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

Product PQRs submitted included those for Levofloxacin, Isoniazid, Ethionamide, Pyrazinamide and others. A random selection was made, and the following reports were briefly checked:

Levofloxacin tablets. Nine batches were produced and released during the review period (2021). Upper and lower control limits were calculated.

Pyrazinamide 400mg tablets. Only one batch was produced during the review period (2021). There were no recalls, OOS results, or complaints. No significant observation was made on data including stability testing data.

Linezolid 600mg tablets. Only one batch was produced during the review period (2021). There were no recalls, OOS or complaints. No significant observation was made on data including stability testing data.

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

Submitted batch manufacturing (and some analytical) records were screened. A few records were selected for review including Levofloxacin 250mg tablets batch LVAH118 and Linezolid 600mg tablets, batch LZAH005, LZAH005B. No significant observations were made.

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

Master documents for manufacturing were submitted for several products. A few were selected for review including Levofloxacin 250mg tablets and Linezolid 600mg tablets. No significant observations were made.

**h) If any of the products are sterile, the completed batch records for the most recent media fill validation that is relevant to the product(s) of interest and report on its outcome:**

N/A

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

One recall was initiated in Germany for Rasagiline 1mg tablets, due to nitrosamine impurity

**j) 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:**

Confirmation was provided, indicating the self-inspections and internal quality audits were performed at regular intervals

**k) 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:**

A copy of the conditional compliance with GMP from UK MHRA was submitted.

**k) Out-of-stock situations:**

The company stated that no out-of-stock situation was expected

**l) Additional documents submitted:**

N/A

| Part 5 | Conclusion – Desk assessment outcome |
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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 ***Micro Labs Limited (Unit 3),*** located at ***Block ML03, 92 SIPCOT Industrial complex, Hosur, Tamil Nadu, 623 126, 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 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-eight Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO TRS No. 986, Annex 2***
   https://digicollections.net/medicinedocs/documents/s21467en/s21467en.pdf

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***
   untitled (digicollections.net)

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://digicollections.net/medicinedocs/documents/s23457en/s23457en.pdf

4. 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***
   9789240020900-eng.pdf (who.int)

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***
   https://digicollections.net/medicinedocs/documents/s21440en/s21440en.pdf

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 TRS No. 1010, Annex 8**
https://digicollections.net/medicinedocs/documents/s23455en/s23455en.pdf

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***
https://digicollections.net/medicinedocs/documents/s20108en/s20108en.pdf

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 TRS No. 961, 957), Annex 1***
https://digicollections.net/medicinedocs/documents/s18681en/s18681en.pdf

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 3.
***Short name: WHO TRS No. 957, Annex 3***
https://digicollections.net/medicinedocs/documents/s22358en/s22358en.pdf

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***
https://digicollections.net/medicinedocs/documents/s19959en/s19959en.pdf

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***
https://digicollections.net/medicinedocs/documents/s18677en/s18677en.pdf

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**
https://digicollections.net/medicinedocs/documents/s18683en/s18683en.pdf

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***
https://digicollections.net/medicinedocs/#d/s21438en

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***
https://digicollections.net/medicinedocs/documents/s18682en/s18682en.pdf

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***
https://digicollections.net/medicinedocs/#d/s20177en/

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***
https://digicollections.net/medicinedocs/#d/s20175en/

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. 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***
https://digicollections.net/medicinedocs/documents/s23697en/s23697en.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***
Essential Medicines and Health Products Information Portal (digicollections.net)

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***
9789240020900-eng.pdf (who.int)

22. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
***Short name: WHO TRS No. 996, Annex 10***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

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***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

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**
https://digicollections.net/medicinedocs/documents/s23699en/s23699en.pdf

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**
9789240020900-eng.pdf (who.int)

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**
9789240001824-eng.pdf (who.int)

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***
https://www.who.int/publications-detail/978-92-4-000182-4

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***
https://www.who.int/publications-detail/978-92-4-000182-4