

WHO PUBLIC INSPECTION REPORT Finished Product Manufacturer
**WHO PUBLIC INSPECTION REPORT
(WHOPIR)**
Finished Product Manufacturer
Part 1: General information

Name of Manufacturer	Micro Labs Limited
Unit number	ML06
Production Block	NA
Physical address	Plot No. S-155 to S-159 & N1, Phase III & IV, Verna Industrial Estate, Verna-Goa, 403722, India
Contact address	Mr SM Mudda smm@microlabs.in
Date of inspection	15 to 18 January 2013
Type of inspection	Routine inspection
Dosage forms(s) included in the inspection	Tablets and Capsules
WHO product categories covered by the inspection	<u>Prequalified</u> HA485 Lamivudine/Zidovudine (150/300) tablets HA 483 Zidovudine 300mg tablets <u>Under assessment</u> HA536 Lamivudine 30mg tablets HA537 Zidovudine 60mg tablets HA555 Lamivudine/Zidovudine (30/60mg) tablets
Summary of the activities performed by the manufacturer	Production and control of finished pharmaceutical products

Part 2: Summary

General information about the company and site

Micro Labs Limited is engaged in manufacturing of medicinal products since 1973. The company is engaged in manufacturing of various therapeutic segments and has a total of 14 manufacturing facilities in India for the manufacture of products for domestic and export markets.

The manufacturing facility, Micro Labs Limited (ML06) is located in Verna Industrial Estate, Verna-Goa, India which is 25km away from main capital city Panaji. The site is engaged in the manufacturing of oral solid dosage forms of medicinal products.

History of WHO and/or regulatory agency inspections

The site was last inspected by WHO in March 2010.

From the Site Master File, it had been noted that the site had been approved by the local drug authority of Goa State, and International Drug Authorities like MHRA, USFDA and Health Canada.

Focus of the inspection

The inspection focused on the production and control of HA485, HA483 (prequalified) and HA536, HA537 and HA555 (under assessment) products. The inspection covered all the sections of the WHO GMP text, including premises, equipment, documentation, materials, validation, sanitation and hygiene, production, quality control and utilities.

Inspected Areas

- Quality assurance
- Good manufacturing practices for pharmaceutical products
- Sanitation and hygiene
- Qualification and validation
- Complaints
- Product recalls
- Contract production and analysis
- Self inspection and quality audits
- Personnel hygiene
- Premises
- Equipment
- Materials
- Documentation
- Good practices in production
- Good practices in quality control.

2.1 QUALITY ASSURANCE

The company had systems in place to ensure the quality of products manufactured. There was an adequately designed and correctly implemented system of quality assurance incorporating GMP and quality control. It was documented and its effectiveness was monitored through audits and self-inspections. All parts of the quality assurance system were adequately staffed with competent personnel, and there were suitable and sufficient premises, equipment, and facilities.

The observations raised from this section have been adequately addressed and will be verified during the next routine inspection.

2.2 GOOD MANUFACTURING PRACTICES (GMPs) FOR PHARMACEUTICAL PRODUCTS

Products were consistently produced and controlled to the quality standards appropriate to their intended use and as required. Systems were in place to reduce the risk of cross-contamination and mix-ups.

The manufacturing processes for the reviewed products were clearly defined and systematically reviewed, and shown to be capable of consistently manufacturing pharmaceutical products of the required quality that comply with their specifications.

The observations raised from this section have been adequately addressed and will be verified during the next routine inspection.

2.3 SANITATION AND HYGIENE

In general, this area was found satisfactory.

2.4 QUALIFICATION AND VALIDATION

Micro Labs Unit ML-06 identified what qualification and validation work was required to prove that the critical aspects of their operations were controlled. Process validation studies were conducted in accordance with the validation policy predefined and approved protocols and written reports summarized the results and the conclusions reached.

The observations raised from this section have been adequately addressed and will be verified during the next routine inspection.

2.5 COMPLAINTS

There was an SOP for handling complaints. All complaints and other information concerning potentially defective products were reviewed according to written procedures and the corrective action was taken.

The observations raised from this section have been adequately addressed and will be verified during the next routine inspection.

2.6 PRODUCT RECALLS

There was a system to recall from the market, promptly and effectively, products known or suspected to be defective. The responsibility to recall the product rests with the Executive Director, Technical and Operations.

2.7 CONTRACT PRODUCTION AND ANALYSIS

Not inspected.

2.8 SELF INSPECTION AND QUALITY AUDIT

A self-inspection programme was in place and was designed to detect any shortcomings in the implementation of GMP and to recommend the necessary corrective actions. Self-inspections were performed routinely (every department audited 2 times/year). A team of qualified auditors was responsible for self-inspections. Recommendations for corrective actions were implemented. The procedure for self-inspection was documented, and there was an effective follow-up programme.

2.9 PERSONNEL

There were sufficient qualified personnel to carry out all the tasks for which the manufacturer was responsible. Individual responsibilities were defined and recorded as written job descriptions. All responsible staff had their specific duties recorded in written descriptions and adequate authority to carry out their responsibilities. The job descriptions reflected were in accordance with the Organization chart.

No temporary workers were employed for activities within the controlled manufacturing areas.

2.10 TRAINING

Training was provided in accordance with a written programme for all personnel whose duties take them into manufacturing areas or into control laboratories. The newly recruited personnel should undergo an induction training covering general (site specific, GMP) and job specific issues. The on-the-job training can be planned (annual plan) and unplanned (implementation of a new procedures, CAPA, etc.).

2.11 PERSONAL HYGIENE

In general, this area was found satisfactory.

2.12 PREMISES

The premises was located, designed, constructed, adapted, and maintained to suit the operations carried out. The layout and design of the premises aimed to minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build-up of dust or dirt, and, in general, any adverse effect on the quality of products. In areas where dust was generated (e.g. during sampling, weighing, mixing and processing operations, packaging of powder), appropriate measures were taken to avoid cross-contamination and facilitate cleaning.

The premises and space was sufficient to carry out various operations on site. It was also noted that the site is under construction to expand the current facility for the production and laboratory. It was also noted that the new warehouse is under qualification.

The observations raised from this section have been adequately addressed and will be verified during the next routine inspection.

2.13 EQUIPMENT

Equipment was located, designed, constructed, adapted, qualified and maintained to suit the operations to be carried out. The layout and design of equipment also aimed to minimize the risk of errors and permitted effective cleaning and maintenance in order to avoid cross-contamination, build-up of dust or dirt, and, in general, any adverse effect on the quality of products. The procedure on the cleaning of equipment and surrounding areas were available.

The observations raised from this section have been adequately addressed and will be verified during the next routine inspection.

2.14 MATERIALS

Materials were sourced from approved suppliers. The address stated on the label of the container didn't contain the Unit number as specified in the approved vendor list. The evaluation of suppliers of active substances, primary packaging materials and printed packaging materials was based on site audits performed at least every 3 years.

All incoming materials were quarantined immediately after receipt until they were released for use or distribution. All materials and products were stored under the appropriate conditions established by the manufacturer and in an orderly fashion to permit batch segregation.

2.15 DOCUMENTATION

Documents were designed, prepared, and distributed with care according to operating procedure. The main data of the operating procedures (title, identification and version code, effective date, expiry date) were entered onto an Excel sheet then printed out

and signed as “Master list of documents” all times when a new document/version was issued.

The majority of standard operating procedures were reviewed regularly (every two years) and kept up to date.

The observations raised from this section have been adequately addressed and will be verified during the next routine inspection.

2.16 GOOD PRACTICES IN PRODUCTION

Production operations followed clearly defined procedures. All handling of materials and products, such as receipt and cleaning, quarantine, sampling, storage, labelling, dispensing, processing, packaging and distribution was done in accordance with written procedures or instructions and, where necessary, recorded.

Deviations from instructions or procedures were avoided, and when deviations took place, these were handled in accordance with an approved procedure.

Checks on yields and reconciliation of quantities were carried out.

The Master Formula Record details the manufacturing instructions. The manufacturing activities performed were recorded in approved batch manufacturing records.

The manufacturing documents and records of product HA555 Lamivudine/Zidovudine (30/60mg) tablets were discussed.

Materials, bulk containers, major items of equipment, and where appropriate, the rooms and packaging lines being used were labelled with an indication of the product or material being processed.

The in-process control tests (friability, disintegration, hardness, loss on drying, leak test) were performed in the IPC laboratory. It was located in the territory of the Production (within the controlled area) but was belonging to the IPQA Department therefore independent of the Production by organization.

2.17 GOOD PRACTICES IN QUALITY CONTROL

Quality control was independent from production.

The quality control unit was concerned with sampling, specifications and testing, and with the organization, documentation and release procedures which ensure that the necessary and relevant tests were carried out and that materials were not released for use, nor products released for sale or supply, until their quality had been judged to be satisfactory. There were 10 persons designated for raw material sampling.

There were adequate facilities, trained personnel and approved procedures were available for sampling, inspecting, and testing starting materials, packaging materials, and intermediate, bulk, and finished products, and for monitoring environmental conditions for GMP purposes. The samples of starting materials, packaging materials, intermediate products, bulk products and finished products were taken by methods and personnel approved of by the quality control department.

The performance of the analytical balances was tested regularly. The weighing was recorded by the attached printer. During the inspection, the verification/calibration protocols and records of analytical balance were discussed. The verification was performed daily, the calibration monthly with certified set of weighs covering the operation range of the balance.

The reference standards, working standards were stored in 2-8 °C. The inventory, certificate, and usage logs of lamivudine and Zidovudine reference materials were available.

The stability chambers (25°C/60%, 30°C/65%, 40°C/75%, 30°C/75%, and, spare) for on-going and accelerated stability studies were available and managed by the QC Department.

The testing of active substances and raw materials were based on quality specifications containing the detailed description of the analytical test methods.

The analytical method validations was performed by the R&D Department (Bangalore), and then transferred to the site. The analytical test methods of the finished products and the majority of the raw materials were validated or in case of compendial methods implemented.

There was periodical calibration and maintenance program in place for analytical instruments. The calibration and maintenance documents of the HPLC were discussed.

Part 3: Conclusion

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, as well as the corrective actions taken and planned, **Micro Labs Limited, ML-06, Plot No. S-155 to S-159 & N1, Phase III & IV, Verna Industrial Estate, Verna-Goa, 403722, India** was considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the WHOPIR, were addressed by the manufacturer, to a satisfactory level, prior to the publication of the WHOPIR.

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