

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

Name of Manufacturer	Mylan Laboratories Limited
Plot number	H-12 and H-13
Production Block	NA
Physical address	MIDC, Waluj Industrial Area Aurangabad, Maharashtra, 431 136, India
Contact address	Same as above
Date of inspection	17 to 20 January 2012
Type of inspection	Initial inspection
Dosage forms(s) included in the inspection	Tablets and Capsules
WHO product categories covered by the inspection	Lamivudine/Nevirapine/Zidovudine 30/50/60 Tablets (HA433) Atazanavir 300mg Capsules (HA477) Atazanavir 150mg Capsules (HA478)
Summary of the activities performed by the manufacturer	Production and control of oral solid dosage forms

Part 2: Summary

General information about the company and site

Mylan Laboratories Limited (hereafter MLL) is the Indian subsidiary of Mylan Laboratories, Inc, USA. MLL Inc USA was founded in 1961 and has a corporate headquarter at Pittsburgh, Pennsylvania, USA. It has operations in North America, Europe and Asia Pacific.

The finished product manufacturing site is located at H-12 and H-13, MIDC, Waluj, Aurangabad, was purchased from M/s Atra Pharmaceuticals Pvt Ltd in September 2010. This unit was constructed in 2008-2010. The facility is designed to manufacture, solid oral dosage forms i.e. Tablets and HG capsules (IR & MR) and conventional tablets, capsules filled with powder, drug layered beads and pellets.

At present the site is under construction to enhance capacity of warehouse, production, quality control and supportive function (technical area, cafeteria) and it will be completed tentatively by March-April 2013.

History of WHO and/or regulatory agency inspections

This was the first WHO inspection of Mylan Laboratories Limited at Waluj, Aurangabad. The site has not been inspected by any of the international agencies except local FDA.

Focus of the inspection

The inspection focused on the production and control of Lamivudine/Nevirapine/Zidovudine 30/50/60mg Tablet (LNZ) and Atazanavir 150mg and 300mg capsules 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
- Sanitization and hygiene
- Qualification and validation
- Complaints
- Recalls
- Self-inspection
- Personnel
- Training
- Personal hygiene
- Premises
- Equipment
- Materials

- Documentation
- Production
- Quality control

2.1 QUALITY ASSURANCE

There was an organization chart and job descriptions specifying the titles and reporting relationships of the various staff. There were documented and approved procedures to guide routine operations and activities. Starting materials, intermediate products, finished goods were controlled and approved by QC/QA before release for use or distribution.

Policies and procedures were in place for qualification and validation of equipment and systems, change control, deviation management, quality risk management and product quality review.

2.2 GOOD MANUFACTURING PRACTICES (GMPs) FOR PHARMACEUTICAL PRODUCTS

Good manufacturing practices were implemented. The necessary resources were generally provided. Manufacturing steps were recorded in batch manufacturing and packaging records. Instructions and procedures were generally written in clear and unambiguous language. Qualifications and validations were performed, adequate premises and equipment were available for production, in-process controls and storage, and operators were trained.

2.3 SANITATION AND HYGIENE

This was generally considered to be acceptable.

2.4 QUALIFICATION AND VALIDATION

The company's approach to qualification, and validation was in general consistent with the WHO technical report series recommendations. The company had identified the qualification and validation work to be performed in their validation master plan.

2.5 COMPLAINTS

Responsible person for handling market complaints was the Head, QA and it was deputised to Manager QA. According to the procedure, where necessary, appropriate follow-up action, possibly including product recall, should be taken after investigation and evaluation of the complaint.

2.6 PRODUCT RECALLS

Responsible person for recall was the Head Quality, deputized by Manager QA or designee. The decision on recall of the defective product should be made within 3

working days (Class I recall), 7 working days (Class II recall) and 15 days (Class III recall) of receipt of the information. Dummy/mock recall was to be carried out once in a year and on change of distribution.

2.7 CONTRACT PRODUCTION AND ANALYSIS

Production activities were not contracted out. Some analysis was carried out on contract basis.

2.8 SELF INSPECTION AND QUALITY AUDIT

Self-inspection was carried out four times in a year for all departments. Audit team members were qualified persons from cross-functional team (Production, QC, QA, Warehouse, Engineering and Human Resources Departments). Check-lists were used to conduct the self-inspection.

There was a procedure for vendor approval and evaluation which provided instructions for vendor audit. It was noted that excipients were qualified based on vendor questionnaire, while APIs were qualified based on vendor questionnaire and on-site audit.

2.9 PERSONNEL

There were organization chart and job descriptions to guide personnel. Most of the personnel interviewed had adequate knowledge and skills to perform assigned duties. It was noted, however, heads of quality control and quality assurance reported separately to Head CQA

2.10 TRAINING

Staff training was performed in accordance with a predefined procedure. Following the impartation of training, staff was assessed through question/answer before being qualified for work.

2.11 PERSONAL HYGIENE

An adequate level of personal hygiene was observed by all those concerned with the manufacturing processes. Direct contact was avoided between the operator's hands and starting materials, primary packaging materials and intermediate or bulk product. Personnel were wearing clean body coverings appropriate to the duties they performed, including appropriate hair covering. Used clothes were stored in separate closed containers.

Personal hygiene procedures included the use of protective clothing for all persons entering production areas.

2.12 PREMISES

In general the buildings and facilities used for manufacture and quality control were located, designed, and constructed to facilitate proper cleaning, maintenance and production operations. Premises were designed to ensure the logical flow of materials and personnel. In-process laboratory was located in the production block. Quality control laboratories were separated from production areas. Sufficient space was given to avoid mix-ups and cross-contamination.

2.13 EQUIPMENT

Balances and other measuring equipment with appropriate range and precision were available for production and control operations and were calibrated on a scheduled basis. Calibration due-date labels were attached to the equipment.

Calibrated standard weights used for in-house checking of balances were available.

2.14 MATERIALS

Starting materials were quarantined, sampled and tested before approval for use. All containers of active pharmaceutical ingredients were sampled individually and tested for identity while full testing was done on a composite sample. Materials were identified by a unique number and tracked using SAP which was also used for material control. However, procedure on the access control and privileges for SAP transactions was not available. The conditions of storage were all controlled and monitored and were generally found to be appropriate for the materials held.

Packaging materials were quarantined, sampled and tested before release for use.

Finished products were not supposed to be released for distribution unless each batch was tested and its production, packaging, testing records and environmental monitoring results were reviewed and found in compliance with GMP and regulatory requirements. Currently, manufacturing site was taking exhibit and validation batches for filing purposes.

2.15 DOCUMENTATION

Documents were designed, prepared, reviewed and distributed with care. In general, documents were approved, signed and dated by the appropriate responsible persons. Documents were laid out in an orderly fashion and were easy to check. Reproduced documents were clear and legible. Documents were regularly reviewed and kept up to date.

2.16 GOOD PRACTICES IN PRODUCTION

The production procedures were established and controlled and had been validated. Production was guided by comprehensive batch manufacturing instructions and records. The various manufacturing stages were performed in effectively segregated

areas. The rooms, equipment and containers were generally appropriately labelled with status, content and stage of processing.

Line clearance checks were conducted before the start of production and packaging. In-process checks, yields and related checks were conducted at the appropriate stages and recorded. Environmental conditions were monitored continuously by settle plates suitably located in production areas.

Readings for ΔP , temperature and relative humidity were taken regularly and recorded in the logbooks.

2.17 GOOD PRACTICES IN QUALITY CONTROL

The QC function was independent from other departments. Samples of starting materials, packaging materials, intermediate products, bulk products and finished products were taken by approved methods. Sufficient samples of starting materials and products were retained to permit future examination of the product.

SOP on the sampling of raw material was reviewed and noted that all containers shall be sampled for identity. AQL was applied for sampling of packaging materials.

Electronic data was readily available for batches tested in 2011. The electronic data was found to match the hardcopy data.

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, *Mylan Laboratories Limited, Waluj, Aurangabad, 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.