

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
Unit number	NA
Production Block	NA
Physical address	Plot No 11, 12 & 13, Indore Special Economic Zone, Pharma Zone, Phase-II, Sector-III, Pithampur-454775 Dist. Dhar, Madhya Pradesh, INDIA
Contact address	Mr Pallab De, Sr. Vice-President, Corporate Quality Assurance, <i>Mylan Laboratories Limited, Plot no. 564 / A / 22, Road no. 92, Jubilee Hills, Hyderabad - 500034, India. Tel: +91-40-30866410, Fax: +91-40-30866699 Mobile: +91-8008001497 Email: Pallab.De@mylan.in</i>
Date of inspection	24, 25 and 26 October 2013
Type of inspection	Initial inspection
Dosage forms(s) included in the inspection	Dispersible tablets
WHO product categories covered by the inspection	HA433 Lamivudine/Nevirapine/Zidovudine 30/50/60mg dispersible tablets
Summary of the activities performed by the manufacturer	Production, packaging, control and release of oral solid dosage forms

Part 2: Summary

General information about the company and site

The facility inspected was Mylan Laboratories Limited, Plot No 11, 12 & 13, Indore Special Economic Zone, Pharma Zone, Phase-II, Sector-III, Pithampur, District Dhar, Madhya Pradesh, India, here after referred to as Mylan Pithampur. The site belongs to Mylan Laboratories Limited, India (the former Matrix laboratories Ltd) with corporate offices at Jubilee Hills, Hyderabad, India which in turn is fully owned by Mylan Laboratories Inc., USA, with headquarters at Pittsburgh, Pennsylvania, USA.

Mylan Laboratories Limited had acquired Unichem Laboratories Limited, Pithampur in March 2013 and currently in a transition phase whereby procedures and systems (such as SAP, LIMS, Documentum, Trackwise and Learning Management System etc) are being implemented from Unichem to Mylan Laboratories Limited. Currently, the site is awaiting WHO prequalification for the variation application before site could start the production activities for commercialization. The site had produced 3 exhibit batches of the product in question together with some other products. Mylan Pithampur is capable to manufacture solid orals (tablets and capsules)

According to the company presentation and SMF, the site employed a total of 106 people as of 24th October 2013 distributed as:

1. Production: 29
2. Quality unit (QA, QC, IPQA, stability): 28
3. Warehouse: 7
4. Engineering: 17
5. Process and packaging development: 5
6. Regulatory affairs: 1
7. Technical services: 4
8. Others (HR, Purchase, Security, Commercial, Finance, EHS, IT, SCM, Projects and OE): 15

History of WHO and/or regulatory agency inspections

This is the first WHO inspection of this site.

Focus of the inspection

The inspection was conducted in relation to a variation application submitted by Mylan to include additional manufacturing site for Lamivudine, Nevirapine, Zidovudine Dispersible 30/50/60mg tablets (HA433). The inspection covered most of 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

There were facilities and procedures for the production and quality control of the products in focus and their level of execution and/or maintenance was generally adequate to ensure products of consistent quality.

At the time of inspection, there was no manufacturing activity carried out. It was noted that hold time study for equipment and product was being performed.

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.

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

2.4 QUALIFICATION AND VALIDATION

Mylan Pithampur identified what qualification and validation work was required to prove that the critical aspects of their operations were controlled. The validation master plan and associated validation protocol and reports were available. Briefly, process validation report of Lamivudine, Nevirapine, and Zidovudine Dispersible 30/50/60mg tablet was reviewed together with batch manufacturing record & batch packaging record.

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.

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 senior management.

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

2.7 CONTRACT PRODUCTION AND ANALYSIS

This is a new manufacturing site acquired by Mylan group. Currently, there was no contract manufacturing carried out at this site. From the site master file, it was noted that some of the analytical tests were outsourced.

This section was 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.

To date no assessments have been carried out

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.

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

2.10 TRAINING

Training was provided in accordance with a written programme for all personnel whose duties take them into manufacturing areas or into quality 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.).

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

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.

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 evaluation of suppliers of active substances, primary packaging materials and printed packaging materials was based on site audits performed periodically.

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.

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

2.15 DOCUMENTATION

Documents were designed, prepared, and distributed with care according to operating procedure. The standard operating procedures were reviewed periodically (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

At the time of inspection, there was no activity being performed inside the production area. It was noted that the hold time study was being conducted for equipment and some of the finished products. The areas were not in operation. No comment on production processes or WIP was possible. All areas operate under a positive airflow relative to the outer service corridor. Throughout the walk round no adverse air pressure differentials were noted. Extra over garments are provided for personnel entering the numerous production suites.

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

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

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, Pithampur, MP, 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.