



**WHO PUBLIC INSPECTION REPORT
(WHOPIR)**

Finished Product Manufacturer

Part 1: General information

Name of Manufacturer	Cipla Ltd
Unit number	Unit I, III, IV, VII
Production Block	N/A
Physical address	Verna Industrial Estate Verna, Salcette, Goa 403 722 India.
Date of inspection	6 and 7 August 2009
Type of inspection	Special
Dosage forms(s) included in the inspection	Oral Dosage Forms
WHO product numbers covered by the inspection	HA043, 049, 053 (Lamivudine) HA039 , 200 (Nevirapine) HA210,267,375,376 (Lamivudine / Nevirapine / Stavudine) HA060 Lamivudine/Zidovudine IN001 (Oseltamivir)
Summary of the activities performed by the manufacturer	Production and control

Part 2: Summary

General information about the company and site

See previous reports - no change to date from the last inspection.

History of WHO and/or regulatory agency inspections

The Goa site was previously inspected by several agencies including the TGA (Australia), MCC (South Africa), MHRA (UK). This site has been inspected by WHO PQ several times before. See company file, reports and WHOPIRS.

Focus of the inspection

The inspection focused on the production and control of selected products as listed above.

Inspected Areas

This was a special inspection, where some systems were being inspected focusing mainly on material management, quality control and documentation.

After arrival, the inspectors introduced themselves and exchanged business cards with company representatives. The inspection team briefly explained the functioning of the prequalification program including assessments, inspections, publication of WHOPIRS and the NOC procedure.

The company made a brief presentation of its activities. This is filed with the report for office use.

Inspectors enquired about the differences in specifications, codes, and batch documents for different markets including WHO, PEPFAR, and India. The company informed the inspectors that this was controlled through different codes for APIs and batch documents by a computer system.

The inspectors requested several documents to start the documentation review. These included for lamivudine tablets, nevirapine tablets and suspension, oseltamivir capsules, lamivudine/nevirapine/stavudine (LNS) (adult, junior and baby) and lamivudine/zidovudine (LZ):

- Annual products quality review reports (APQR)
- API specifications,
- Batch records
- Validation protocols and reports and source data;
- Complaints register
- Deviations register
- Change control register
- Code change management SOP and record
- SOPs
- Analytical reports



- Stability study protocols

It was noted that various APIs had undergone several changes in codes for use in various batches of product.

It was verified that the approved APIs were used in batches produced and supplied as WHO prequalified products. In addition, the approval of the additional manufacturing sites for APIs, as applied for through the variations guideline, was verified.

The computer system was inspected to establish the code numbers for the various APIs. Checks were made to verify which code API was used in which batches of products. It was noted that various changes or code transfers were made.

As some chromatograms for a product (validation samples) reflected identical retention times, and the peaks appeared essentially identical, these were checked and verified in the QC laboratory against the electronically stored chromatograms. Selected individual chromatograms were retrieved and overlaid. These were found to be acceptable.

Stability testing

Stability testing schedules and protocols were inspected for selected products and batches. Tabulated data was verified against source data and chromatograms were inspected. In selected cases the assay values were manually calculated to verify reported values.

A quick visit to Unit III was made where the following was briefly inspected:

- material storage,
- labeling of materials including status,
- sources of materials,
- separation and segregation;
- cleanliness,
- dispensing area with associated logs for the day,
- production area including granulation 1 and compression where in process checks were checked on the BMR,
- secondary packaging lines for line clearance and in process checks in BPRs.

Other documents reviewed:

- Approved vendors list for selected APIs
- SOP CQA-279 "Handling of raw materials for specific requirements"
- FPP specifications
- Deviation approval form DV8/0/014 "Code transfer"
- Specimen signature of staff members
- SOP QCP-59 "Sampling and analysis of raw materials (for WHO)"
- SOP CQA-28 "Evaluation and approval of manufacture"

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, Cipla Ltd

Goa, India was considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

Part 4: References

1. *Quality Assurance of pharmaceuticals. A compendium of guidelines and related materials. Volume 2, Second updated edition. Good manufacturing practices and inspection.* World Health Organization, Geneva, 2007
http://www.who.int/medicines/areas/quality_safety/quality_assurance/production/en/index.html
2. WHO Good Manufacturing Practices: water for pharmaceutical use. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report.* Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 3
http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf
3. 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
http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf
4. Supplementary guidelines on good manufacturing practices for heating, ventilation and air-conditioning systems for non-sterile pharmaceutical dosage forms. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report.* Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 2
http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf
5. 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
http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf
6. Good Practices for National Pharmaceutical Control Laboratories. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-sixth Report.* Geneva, World Health Organization, 2002 (WHO Technical Report Series, No. 902), Annex 3.
http://whqlibdoc.who.int/trs/WHO_TRS_902.pdf#page=37