



**WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Finished Product Manufacturer**

Part 1: General information

Name of Manufacturer	Universal Corporation Ltd.
Physical address	Universal Corporation Ltd. Club Road, Plot No. 13777, P.O. Box 1748-00902, Kikuyu Town, Kenya.
Date of inspection	13-16 June 2011
Type of inspection	Follow-up inspection
WHO product numbers covered by the inspection	HA490
Summary of the activities performed by the manufacturer	Production, quality control, storage and distribution of finished pharmaceutical products

Part 2: Summary

General information about the company and site

The Universal Corporation Ltd. manufactures tablets, capsules, liquids, creams and ointments and was located in the town of Kikuyu, about 37 km away from the Nairobi international airport.

The company had many products registered in the following countries:

- Kenya: 192,
- Malawi: 46,
- Burundi: 36,
- Sierra Leone: 33,
- Zambia: 37,
- DR Congo: 30,
- Uganda: 9,
- Ethiopia: 2,
- Tanzania: 4.

The site had an annual production capacity of 4.8 billion tablets, 79 million capsules as well as 2.8 million bottles of 10 mL-100 mL liquids, 12.5 million 5 L bottles, 20 million tubes, 22 million sachets.

History of WHO and/or regulatory agency inspections

The site has also been approved by the regulatory authorities of Tanzania, Uganda and Ethiopia.

The site was previously inspected by the WHO prequalification programme in May 2010.

Focus of the inspection

This inspection focused on a review of the corrective and preventive actions from the last inspection, on data verification on the production and control of Lamivudine/Zidovudine 150 mg/300 mg tablets (HA490, referred to under its commercial name Lamoqid in the rest of the report) and on each of the following 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.

Inspected Areas

Day 1

The inspection was started with an opening meeting. After introductions and a brief company presentation, inspectors proceeded to the review of the following documents:

- Product quality reviews (PQRs).
- Certificates of analyses (COAs) selected products manufactured at the site.
- Batch manufacturing records (BMRs) and example of a deviation report.
- Specifications and COAs for Ibuprofen.
- Selected out-of-specification (OOS) reports
- Change control Procedure.
- Training record on the revised specifications and test procedures for Lamosid tablets.
- Change control examples and change control register for 2011.
- Job descriptions for selected members of staff.
- Register for rejects.
- Product destruction records.
- SOP on Waste Management and Disposal.
- SOP on "Handling of Out of Specification Results".
- SOP on Approval and Rejection of Raw Materials.
- SOP on failure investigation.
- SOP "Deviation control procedure"
- Deviation management for several batches in 2010 and 2011 together with the BMR's and analytical test results from the affected batches.
- SOP Re-Processing/Re-work procedure.
- SOP for the CAPA procedure.

Day 2

After giving a list of the observations of the previous day, inspectors proceeded to the review of documentation and to a visit of the QC laboratory.

Inward sample storage- examination of samples awaiting testing.

- Analytical reports for selected batches.
- Logbooks for the use of Waters 1 and 2 HPLC systems.
- Data from Lamosid pilot batch manufactured in 2009.
- Column system suitability testing sheets.
- Comparative dissolution study protocol



- Report for the biowaiver for Lamoqid tablets and associated analytical reports.
- Certificate for reference standard.
- Forms for calibration of comparative dissolution testing apparatus.
- Apparatus used for performance verification and calibration of dissolution testing apparatus.
- Stability data for Lamoqid at the 18 month timepoint.
- Stability chamber loading logbook for the 30°C/75%RH chamber.
- Data stored on the Star system for dates from July 27 to July 31st. Runs of interest were printed off.
- BMR and handling of OOS results.
- Deviation report regarding the absence of standard injections prior to the run.
- HPLC usage logbook.
- Reference standard storage refrigerators (2-8°C) and reference standards.
- Data for FTIR for Sulfamethoxazole BP API.
- Retention samples for lamivudine and zidovudine API batches.
- Daily temperature and humidity monitoring records for the retention sample area.
- Qualification data for lamivudine working reference standard.
- Handling of complaints, actual SOP, complaint register, documentation for major complaints from 2010.
- Procedure for product recalls.
- Product recalls.
- Purified Water system (layout, maintenance, sanitisation) and water monitoring.
- Environmental monitoring (monitoring by settle plates, particle monitoring).

Day 3

After giving a presentation of the observations from the previous day, inspectors proceeded to the visit of the following areas:

- Material receiving bays.
- Sampling areas (examined through glass viewing panes).
- Warehousing areas for storage of packaging materials and starting materials (separate areas were used for quarantined and released materials).
- Rejects storage room.
- Production ground floor: this included an overview of each room involved in the manufacturing of Lamoqid (blending room 2, granulation, fluid bed drying and milling room 1, tablet pressing room 7, change parts storage room, coating room 1, coating solution preparation room, primary and secondary packaging, etc.)
- Finished goods warehouse.
- HVAC system for production area (concept, filter status, AHU's, pressure differences in between rooms in production area).
- Water plant and pipeline (loop) system.
- Compressed air generation system.

Day 4



Inspectors reviewed the following documents:

- Validation Master Plan.
- List of equipment qualification status.
- Validation status of products.
- Validation plan for year 2011.
- Bracketing of equipment for cleaning validation.
- Risk assessment for solid oral products.
- Questionnaire for cleanability interview.
- Cleaning validation protocol for a multimill.
- SOP entitled "cleaning of multi mill change parts".
- Cleaning validation method report.
- Records of the loading of Lamozid on July 9, 2009, stored in HDPE bottles, in the 30°C/75%RH chamber.
- Batch packaging records for Lamozid.
- Method verification report for related substances of lamivudine.
- Training records for a member of staff.
- List of SOPs.
- Failure mode and effects analysis (FMEA) for Lamozid.
- Impact assessment document for the oral dosage facility.
- SOP on "environment, health and safety risk management."
- Register for out-of-specification results (OOS's).
- Handling out-of-specification results.
- Example of an OOS investigation report.
- Quality risk management procedure.
- Self-inspection procedure.
- Handheld raman equipment installation and operational qualification.
- BMRs.
- SOP on sampling procedure for non-sterile raw materials.
- Manufacturing area and equipment for tablets in the 1st floor
- HVAC qualification, with an emphasis on the company's determination of pressure differentials in between the rooms in the production area.
- Usage and monitoring of raw water in production area.
- Qualification of the compressed air system.
- Personnel Training (SOP, training schedule 2011).
- Training record microbiologist.

2.1 QUALITY ASSURANCE

The company had systems in place to ensure the quality of products manufactured. A comprehensively designed system of quality assurance incorporating GMP and quality control was generally implemented and maintained.

Product Quality Review (PQR)

PQRs were prepared in accordance with the SOP for Product Quality Review. According to this SOP, the aim of the implementation of the PQR was to provide assurance that process performance and product quality are managed over its lifecycle. PQR data entry form and PQR summary templates were prepared.

The product under assessment was not yet commercially manufactured and therefore its PQR was not available. PQRs were reviewed for other products as a basis for assessment of their adequacy.

Deviation management

Deviations and incidents were handled according to a documented procedure. Deviation and incident records were maintained in a register.

Change Control

Change controls were managed according to a documented procedure.

Out-of-specifications

Issues, which were noted regarding the investigation of out-of-specification results, were corrected in the company CAPAs. Their effective implementation will be verified during the next inspection.

2.2 GOOD MANUFACTURING PRACTICES (GMPs) FOR PHARMACEUTICAL PRODUCTS

All necessary resources were provided, including

- appropriately qualified and trained personnel;
- adequate premises and space;
- appropriate materials, containers and labels;
- approved procedures and instructions;
- suitable storage and transport;
- adequate personnel, laboratories and equipment for in-process controls.

Instructions and procedures were written in clear and unambiguous language, specifically applicable to the facilities provided. In most cases, operators were trained to carry-out procedures correctly.

2.3 SANITATION AND HYGIENE

This topic was not specifically covered during this inspection, but no significant concerns were identified. The hygiene measures in place appeared to provide sufficient assurance of the prevention of contamination.

2.4 QUALIFICATION AND VALIDATION

A version of the master validation plan dated November 27, 2010, was presented.

A list of equipment qualification status was available.

2.5 COMPLAINTS

The handling of complaints was specified in a written procedure. The complaints register was maintained. A person responsible for the handling of complaints was designated (QA manager). His duties were delegated to the deputy QA manager. Attention was given to counterfeiting. Provisions existed for the initiation of a recall, if required. Complaints were classified into three categories: Critical, Major, and Minor.

2.6 PRODUCT RECALLS

There was a system to recall the products from the market. A recall committee was defined and included relevant personnel. The head of QA was responsible for the final recall decision. Recalls were classified as: Class I, Class II, and Class III.

In the absence of recalls, a mock recall should be carried out every two years according to the company SOP. A recall should be completed within 30 working days if distributed on the Kenya market. If the product was exported, the timeline should respect country rules.

2.7 CONTRACT PRODUCTION AND ANALYSIS

This area was not covered during this inspection.

2.8 SELF INSPECTION AND QUALITY AUDIT

Self-inspections were performed in accordance with the company's SOP. The self-inspection results were documented.

2.9 PERSONNEL

Individual responsibilities were clearly defined and understood by the persons concerned and recorded as written descriptions.

2.10 TRAINING

There was a SOP for personnel training in place.

2.11 PERSONAL HYGIENE

Personnel gowning appeared to be appropriate. Hand washing was performed before entering production areas and signs to this effect were posted.

2.12 PREMISES

Premises were located, designed, constructed and adapted to suite the operations carried out. The layout and design of the premises was aimed at minimizing the risk of errors and allowed for 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.

2.13 EQUIPMENT

Focus was placed on equipment located on the ground floor and a short visit was made to the 1st floor.

Purified water system

A new water system was in use since June 2011 and had been connected to the old loop system.

Key sampling points were defined and were checked daily and weekly for physical/chemical tests and microbial tests (weekly). Tests were performed in accordance with BP procedures with alert, action and maximum limits specified.

Compressed dried air (CDA)

The compressed air generation unit was installed outside the building and was found to be acceptable.

2.14 MATERIALS

The management of starting materials, finished products and their storage was found to be appropriate in general.

2.15 DOCUMENTATION

Documents were designed, prepared, reviewed and distributed. Documents were approved, signed and dated by the appropriate responsible persons. Documents were laid out in an orderly fashion and were easy to check in general, but details were lacking in certain cases. These issues were generally resolved in the CAPAs submitted by the company.

2.16 GOOD PRACTICES IN PRODUCTION

Handling of materials and products, and measures to prevent mix-ups and cross-contamination were in place and generally acceptable. However, issues were raised regarding the company's policy for reprocessing-reworking as well as regarding holding times for in-process intermediates. These issues were adequately addressed by the company's revised SOP and will be further verified during the next inspection.

2.17 GOOD PRACTICES IN QUALITY CONTROL

Organization, documentation and release procedures were in place to ensure that the necessary and relevant tests were carried out.

There were adequate facilities, personnel, approved procedures for sampling, inspecting and testing of starting materials, packaging materials, etc. Records were made demonstrating activities performed.

Recent improvements were noted to have been made with updated procedures, new software and analytical equipment, as well as staff training.

Part 3: Conclusion

Based on the facilities inspected, the personnel 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, *Universal Corporation Ltd., Club Road, Plot No. 13777, Kikuyu, Kenya*, was considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

All of the non-compliances observed during the inspection which 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. The full implementation of the corrective and preventive actions will be verified during the next inspection.

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