WHO PUBLIC INSPECTION REPORT Finished Product Manufacturer

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(WHOPIR)

Finished Product Manufacturer

Part 1: General information

Name of Manufacturer	**Cipla Quality Chemical Industries Limited**
Unit number	No specific unit number specified
Production Block	There is currently only 1 production block at the specified address
Physical address	Plot 1-7 Luzira Industrial Park, P.O BOX 34871, Kampala, Uganda
Contact address	Mr Nevin Bradford Chief Executive Officer NBradford@ciplaqcil.co.ug
Date of inspection	3 to 6 November 2015
Type of inspection	Routine GMP inspection
Dosage forms(s) included in the inspection	Tablets
WHO product categories covered by the inspection	HA039 Nevirapine 200 mg tablets HA060 Lamivudine/Zidovudine 150/300 mg tablets MA064 Artemether/Lumefantrine 20/120 mg tablets HA352 Efavirenz 600 mg tablets HA365 Lamivudine/Zidovudine/Nevirapine 150/300/200 mg tablets HA489 Lamivudine/Tenofovir Disoproxil (fumarate) Tablet, Film-coated 300mg/300mg
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

Quality Chemical Industries Limited (hereafter CiplaQCIL) was founded in 2005 as a Joint Venture between QCL, a local regional manufacturer and major distributer and Cipla of India. According to the company presentation materials the company was established with a vision to become a center of excellence in a regional manufacturing of Quality, Affordable and Newer medicines. Commercial production was launched in 2009, and in 2014, QCIL rebranded to Cipla QCIL due to the increase from 35% to 51% of Cipla's stockholding in the JV company in November 2013.

The site was located at Luzira Industrial park about 2 km from Luzira city and about 10 km from Kampala.

The main pharma plant consists of four floors:

- Lower ground floor - Administration area and canteen facility
- Ground Floor - Change rooms for visitors, gents and ladies, Quality Assurance, Training Hall, Stability Chambers, Control Sample Room, Raw material Store, Rejected material stores, Packing material Store, dispensing and sampling area and Finished goods Store
- First Floor – All manufacturing, packing and Quality Control activities
- Second Floor – Service and utilities equipment are installed on this floor to provide for the whole plant

Only tablets are produced. The facility had three granulation suites, three blister lines and one bottle packing line. The facility is modelled around the Cipla, Unit III facility in Goa and design work was performed by the same organisation. The lab was equipped with ten HPLC and one GC and the company advised that most of the tests for WHO PQ products were carried in-house, but the company does have three contract laboratories that are used to perform certain limited testing. The current capacity of the plant is 80 million tablets per month. Biometric access to the facility is provided and three lifts are used for material movement.

The company has both wet and dry granulation technology products. Duovir and Nevimune are produced using dry compaction method, whereas Duovir N, Efavir, Duomune, and Lumartem require wet granulation. Duomune is a bi-layered tablet. Lumartem is packed in blister pack whereas rest of all tablets are packed in containers.

It was noted that majority of the products manufactured purchased by and supplied to the Ugandan national medical stores. These products are differentiated from private market products by the inclusion of embossing of "UG" on the tablets.

History of WHO and/or regulatory agency inspections

The manufacturing site was first inspected by WHO-PQT in January 2010, and the last WHO-PQT inspection was performed in September 2012.

Focus of the inspection

The inspection focused on the production and control of finished pharmaceutical products:

- Nevirapine 200mg tablets
- Lamivudine/Zidovudine 150/300mg tablets
- Artemether/Lumefantrine 20/120mg tablets
- Efavirenz 600mg tablets
- Lamivudine/Zidovudine/Nevirapine 150/300/200mg tablets
- Lamivudine/Tenofovir Disoproxil (fumarate) Tablet, Film-coated 300mg/300mg

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
- Qualification and validation
- Complaints
- Recalls
- Supplier qualification
- Premises
- Equipment
- Materials
- Documentation
- Production
- Quality control

2.1 PHARMACEUTICAL QUALITY SYSTEM

An adequately comprehensive documented pharmaceutical quality system was generally, implemented across the manufacturing site. Production and control operations were specified in written form and GMP requirements were generally followed. Managerial responsibilities were specified in job-descriptions. The organisation chart was available and reviewed.

Product Quality review was conducted based on a corporate procedure. The procedure for risk management was in place and it was stated that it had been applied in various areas including validation, change control and management of deviations.

Although from its establishment the company had used much from the knowledge and expertise gained from the Cipla arm of the partnership, it wasn't until 2014 when Cipla became majority stakeholders that a more formal and comprehensive incorporation into the Cipla manufacturing network commenced. At the time of the inspection, some Cipla corporate procedures were still being rolled out to the site and others were not yet fully implemented. The company was able to show that there had been much progress in this extensive project and advised that the remaining policies and procedures would be implemented within 6-8 months' time. It was claimed that most of the equipment are of same make as being used in Cipla India and this was confirmed to be the case from that seen during the product area part of the inspection.

The actions taken or proposed to be taken in relation to the deficiency pertaining to quality assurance have been considered acceptable and their satisfactory implementation will be verified during future inspections.

2.2 GOOD MANUFACTURING PRACTICES (GMPs) FOR PHARMACEUTICAL PRODUCTS

Good manufacturing practices generally were implemented. Necessary resources were provided, including qualified and trained personnel, adequate premises, suitable equipment and services, appropriate materials, containers, approved procedures and instructions, laboratories and equipment for in-process and other controls. Qualification and validation were performed. Manufacturing steps were recorded in batch manufacturing and packaging records. Manufacturing processes were defined and reviewed. Product was released by the authorized persons.

The actions taken or proposed to be taken in relation to the deficiency pertaining to GMP for pharmaceutical products have been considered acceptable and their satisfactory implementation will be verified during future inspections.

2.3 SANITATION AND HYGIENE

In general, premises and equipment were maintained at a satisfactory level of cleanliness. The company had a standard operating procedure as the basis for its approach to personal hygiene and sanitation in its production facility.

2.4 QUALIFICATION AND VALIDATION

The company's overall validation policy was described in a Validation Master Plan and SOP for Process Validation. The company identified what qualification and validation work was required. The key elements of a qualification and validation programme were defined and documented in a validation master plan.

2.5 COMPLAINTS

Complaints were handled according to a SOP. There were no changes made to complaint procedure since the last WHO inspection. It was also noted that the company did not receive any complaint for any of the WHO prequalified products since the last WHO inspection.

2.6 PRODUCT RECALLS

A SOP described the procedure for handling recalls. There were no changes made to recall procedure since the last WHO inspection. It was also noted that the company did not recall any WHO prequalified products since the last WHO inspection.

2.7 CONTRACT PRODUCTION AND ANALYSIS

Production operations were not contracted out. Some analytical tests were contracted out to contract laboratories. This was not covered by this inspection due to the time constrained.

2.8 SELF INSPECTION AND QUALITY AUDIT

Self-inspection was not covered by this inspection.

2.9 PERSONNEL

The manufacturer had an adequate number of personnel with the necessary qualifications and practical experience. Responsible members of staff and their specific duties were recorded in written job descriptions. An organization chart was available.

Job descriptions for key staff QA, QC manager and production head were reviewed and they were generally considered to be satisfactory.

The actions taken or proposed to be taken in relation to the deficiency pertaining to personnel have been considered acceptable and their satisfactory implementation will be verified during future inspections.

2.10 TRAINING

Personnel's training was conducted according to a SOP. Members of Staff were required to undergo induction training and on job training. Detailed specific training required for analyst qualification was considered to be appropriate.

Requirements for ongoing training were included in the SOP and there was Training Plan for 2015. Training effectiveness was required to be evaluated. Assessment was by questionnaire and/or written test.

The actions taken or proposed to be taken in relation to the deficiency pertaining to training have been considered acceptable and their satisfactory implementation will be verified during future inspections.

2.11 PERSONAL HYGIENE

The necessary requirements were fulfilled. Full gowning was in use in the grade D production areas. All changing rooms were provided with SOPs with clear photographs which pictorially described the gowning procedures. The approach to sanitation and hygiene was acceptable in general.

The actions taken or proposed to be taken in relation to the deficiency pertaining to personal hygiene have been considered acceptable and their satisfactory implementation will be verified during future inspections.

2.12 PREMISES

Manufacturing areas and the QC laboratory were generally of a good standard. Pressure differentials between each zone and manufacturing rooms were monitored. 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. Quality control laboratories were separated from production areas.

The actions taken or proposed to be taken in relation to the deficiency pertaining to premises and utilities have been considered acceptable and their satisfactory implementation will be verified during future inspections.

2.13 EQUIPMENT

Equipment was generally of a good standard, clean and well maintained. Equipment was not dedicated in general.

The actions taken or proposed to be taken in relation to the deficiency pertaining to equipment have been considered acceptable and their satisfactory implementation will be verified during future inspections.

2.14 MATERIALS

In production, dispensed starting material and intermediate products were identified during the different production stages using proper labels that include the identity and status of each material or product. Materials were obtained from approved suppliers.

The actions taken or proposed to be taken in relation to the deficiency pertaining to materials management have been considered acceptable and their satisfactory implementation will be verified during future inspections.

2.15 DOCUMENTATION

Document control was generally effective as Company had an approved procedure for control of documents.

The actions taken or proposed to be taken in relation to the deficiency pertaining to document control system have been considered acceptable and their satisfactory implementation will be verified during future inspections.

2.16 GOOD PRACTICES IN PRODUCTION

There were provisions in place to regularly clean the production equipment and premises (floors, ceilings, etc.). Dust extraction systems were in place to prevent accumulation of dust resulting from the various production activities (sifting, sieving, and compression). The controls in place were generally considered rigorous.

Processing operations were adequately performed. Only one product was manufactured in each room at any one time.

Primary packaging operations were inspected in process for the filling of boxes. Modern, state-of-the-art equipment was in place with controls for tablet count, bottle weight, labelling and metal contamination. Only one product and batch was packaged in a primary packaging room at one time and adequate procedures for line clearance were in place.

The actions taken or proposed to be taken in relation to the deficiency pertaining to production areas have been considered acceptable and their satisfactory implementation will be verified during future inspections.

2.17 GOOD PRACTICES IN QUALITY CONTROL

Starting materials were sampled and tested.

Approved specifications and reference specimens were available.

Out of specifications (OOS) test results were handled according to a SOP. The procedure was reviewed and discussed. Non-compliances observed during the inspection that were listed in the full report regarding the OOS investigation procedure were addressed by the manufacturer to a satisfactory level.

The specifications, HPLC test method for assay, worksheets, test records and equipment maintenance were available for inspection. Tests followed the instructions given in the relevant written test procedure.

The QC laboratory visit also included an inspection of reference substances, stability studies and data integrity.

The actions taken or proposed to be taken in relation to the deficiency pertaining to quality control laboratory have been considered acceptable and their satisfactory implementation will be verified during future inspections.

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, **Cipla Quality Chemical Industries Limited, Kampala, Uganda** 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.