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WHO PUBLIC INSPECTION REPORT (WHOPIR) Quality Control Laboratory

Part 1: General information

Name of QC Laboratory	**National Quality Control Laboratory (NQCL)**
Physical address	Hospital Road KNH Complex P.O. Box 29726-00202, KNH Nairobi, Kenya
Contact person and email address.	Dr Hezekiah K. Chepkwony, Director, hchepkwony@nqcl.go.ke
Date of inspection	24 to 26 June 2015
Type of inspection	Routine inspection
Type(s) of testing included in the inspection	Physical, chemical, instrumentation and microbiology
Summary of the testing activities performed by the QC Laboratory	

Type of analysis	*Finished products*	*Active pharmaceutical ingredients*
Physical/ Chemical analysis	• pH • Loss on drying • Water content • Friability • Disintegration • Dissolution • Density	• pH • Loss on drying • Water content • Density • Melting point
Identification	• FTIR • HPLC (UV-Vis detection) • AAS • UV-Vis spectrophotometry	• FTIR • HPLC (UV-Vis detection) • AAS • UV-Vis spectrophotometry.
Assay, impurities and related substances	• HPLC (UV-Vis detection) • UV-Vis spectrophotometry • AAS • Volumetric titrations • Polarimetry • Microbial assay Determination of related substances/ impurities and degradation products.	• HPLC (UV-Vis detection) • UV-Vis spectrophotometry, • AAS • Volumetric titrations • Polarimetry • Microbial assay • Determination of related substances/impurities and degradation products.

	Microbiological tests	• Sterility test • Microbial purity • Bacterial endotoxins test (LAL)	• Microbial purity	
	Stability studies	Not applicable	Not applicable	

Part 2: Summary

General information about the company and site

The **National Quality Control Laboratory of Kenya** (hereafter referred to as NQCL) located in Nairobi, was inspected by a WHO prequalification inspection team on 24 – 26 June 2015.

The NQCL was set up in 1978 as Drug Analysis & Research Unit (DARU), housed at the then University of Nairobi, Faculty of Pharmacy and was facilitated by the Ministry of Health (MoH). In 1985, MoH incorporated a specific QC laboratory as part of the National Drug Policy. In 1992, the Government of Kenya through an Act of Parliament (CAP 244 Section 35D, Pharmacy & Poisons (Amendment) Act, 1992) established the Laboratory as a legal entity. In 1993-1994, GTZ reached an agreement with the Kenyan Government to renovate the facility and equip the laboratory at its present location. In 1994-1999, NQCL was run jointly by GTZ and the Kenyan Government. In 1999, full operation of the laboratory was handed over to the Kenyan Government. In March 2005, NQCL initiated participation in newly established WHO laboratory pre-qualification program. In July 2008, NQCL attained WHO Pre-qualification status. The NQCL became the first public institution in East, West and Central Africa to be thus recognized.

The role of NQCL is ensuring standards and checking quality of drugs & medicinal substances by performing physical, chemical, biological and other pharmaceutical evaluation of drugs and medicinal substances. The NQCL inform the Government through the Poison & Pharmacy Board (PPB) of the results of such tests so that appropriate action can be taken if products do not comply with set specifications for safety and effectiveness. Also, NQCL contributes to the overall Ministry of Medical Services' mandate of "delivery of quality healthcare services to all Kenyans".

It was noted from the opening meeting presentation that 45 staff plus contracted staff around 20 were employed by NQCL. Most of the qualified staff were pharmacists and chemists by their training. The laboratory was equipped with 8 HPLC systems and performs microbial limit test (MLT), bacterial endotoxin test (BET), and microbiological assay and bought new isolators for sterility test after the last WHO PQ inspection.

History of WHO and/or regulatory agency inspections

NQCL had been pre-audited by a WHO prequalification team on 25-26 July 2005, after which a status overview of corrective actions had been received, dated 8 August 2006. A pre-inspection had been performed by a WHO prequalification team on 10-11 May 2007. The laboratory was inspected by WHO in April 2008 and in August 2011. From the opening meeting presentation, it was noted that NQCL is currently pursuing ISO 17025 accreditation wet chemistry (accreditation currently ongoing).

Inspected Areas

The following areas of the WHO good practices for the pharmaceutical quality control laboratories were covered in this inspection:

- Organization and management
- Quality management system
- Control of documentation
- Records
- Data-processing equipment
- Personnel
- Premises
- Equipment, instruments and other devices
- Reagents
- Reference substances and reference materials
- Calibration, verification of performance and qualification of equipment, instruments and other devices
- Traceability
- Incoming samples
- Analytical worksheet
- Validation of analytical procedures
- Testing
- Evaluation of test results
- Certificate of analysis
- Retained samples
- Safety
- Microbiological testing

List of persons (and their positions) met during the opening/closing meeting

- H. K. Chepkwony, Director
- Ernest Mbae, Deputy Director, Technical Services
- Serah Muteru, QA Manager
- Sarah Mwangi, Pharmacist, GMP Unit
- David Moenga, Deputy Head QA
- Francis Naula, Analyst
- Jeffrey Kalama, Deputy Head Instrumentation
- Clement Mwangi, Analyst
- Peter Omwancha, Clerical officer
- Eric Mutua, Analyst
- Josephine Onyango, Executive Secretary
- Michael Bugigi, Deputy Head, wet chemistry
- Eric Ngamau, Analyst
- Emmanuel Tanui, Head Biological Analysis Unit
- Mathayo Kwena, Head, Wet Chemistry & Instrumentation
- Serfine Abade, Laboratory Technician
- Mecry Wandeto, Deputy Head Microbiology
- Gladys G. Bogonko, Analyst

- Rebecca Manani, Head Documentation Unit
- Beatrice Mutisya, Lab Technologist
- George Wang'ang'a, Deputy Director F&A
- Khadija Hassan, Analyst
- Jane Matundura, Lab Technologist

2.1 Organization and management

The NQCL had the managerial and technical personnel and resources needed to carry out their duties. The organization of the laboratory was defined in an organization chart. The responsibilities of personnel were defined in job descriptions.

The Quality Manual was briefly reviewed by the inspector and included following sections:

- Quality Policy Statement
- Quality System Objectives
- Management Requirements (organization, management system, document control & management, purchasing, services & supplies, complaints, corrective action, preventive action, internal audits and management reviews)
- Technical Requirements (personnel, facility, test method, method validation & verification, equipment, measurement traceability, sampling etc)

The records were kept for all incoming samples manually. The records of incoming samples were logged in a sample register. Samples were supplied together with analytical request forms. The samples were inspected on receipt and appropriately stored until testing started.

Internal audits were carried out once per year according to the check list, findings were recorded to the report and CAPAs proposed. The resulting reports were approved by the Director.

2.2 Quality management system

The QMS was based on WHO Good Practices for Pharmaceutical Quality Control laboratories (GPPQCL) and ISO 17025-2005 guidelines. The elements of the quality management system were documented in the quality manual.

The SOP for carrying out an internal audit of quality systems was reviewed.

A training record of two of the internal auditors selected for 2015 internal audit was reviewed and noted that the Kenya Accreditation Service / KENAS provided an on-site training on 14th July 2014 to around 20 staff on internal audit course based on ISO/IEC 17025:2005. Those who passed the course were given certificate with "successfully completed" whereas rest of the staff were given certificate with "certificate of participation". The assessment records were retained by KENAS.

Management review (MR) meetings were carried out once a year. In addition, monthly management meeting was carried out with the Unit Heads. The SOP for MR meetings was available. The procedure for management review meeting included suitability of the policies, procedures, reports from managerial & supervisory personnel, outcome of recent internal audit, external inspections, complaints, CAPA, results of intra-laboratory results or proficiency test etc. The minutes of last MR meeting held in September 2014 were reviewed and found to be adequate. It was recommended to include OOS, change controls, deviations, documentation etc at the MR meetings.

The issues raised from this section have been satisfactorily addressed, and will be verified during future inspections.

2.3 Control of documents

The laboratory has a paper based documentation system. The SOP for control of documents was reviewed and noted that SOP provided procedure on the control of documents. The SOPs were reviewed every 2 years, and as and when there was a need to do so. The SOP for writing of SOP was reviewed which provided instructions on how an SOP can be drafted, including SOP number, version number, formatting, table of content (TOC), classification of SOP into technical & administrative, issuance of SOP and changes in SOP as minor and major changes. In general, the procedure was found satisfactory. It is recommended to make a template of the logbook as part of the SOP.

The issues raised from this section have been satisfactorily addressed, and will be verified during future inspections.

2.4 Records

The standard analytical worksheets were used and archived. The original observations, including calculations and derived data, calibration, validation and verification records and final results, were retained on record and were available for review.

2.5 Data-processing equipment

The laboratories were fitted with automated analytical instruments. Most were loaded with off the shelf validated software (e.g. Shimadzu’s LC solution, Agilent’s Chemstation and Merck Hitachi’s HSM Manager). Access to analytical data processing equipment was controlled via individual usernames and passwords.

The issues raised from this section have been satisfactorily addressed, and will be verified during future inspections.

2.6 Personnel

The NQCL had adequate numbers of qualified staff to conduct the assigned responsibilities. It was noted that there were total of 45 staff working in the lab, around 20 of the staff on two year contract (lab analyst, subordinate staff, procurement and finance) and rest 25 were pharmacists from the ministry of health.

The SOP for carrying out laboratory training was reviewed and noted that all new staff member trainees and students were provided with training for 60 working days in different lab sections. At the end of the training, students will write a report which was not applicable to the new staff. For new staff, a competence evaluation was conducted through a written examination where new staff had to score above 75% marks and also analyse blind sample. Based on the acceptance of these two aspects, a trainee was qualified and job description (JD) was finalized. Validation and Uncertainty of measurement was reviewed and noted that the Kenya Bureau of Standards / KEBS provided this training and certificate was issued to each participants. The participants were given printout of the presentation as well as copy of the ISO 17025 standard.

The issues raised from this section have been satisfactorily addressed, and will be verified during future inspections.

2.7 Premises

The laboratory was broadly divided into two wings, one for the chemical, physical and instrumentation testing whereas another wing was responsible for microbiological testing which included microbial limit test (MLT), sterility testing, storage of cultures, media etc. They all had adequate space and in general were found to be clean and tidy. It is understood from the discussion that laboratory will move out from its existing location but not sure how soon.

It was noted that laboratory uses type 1 and type 2 Grade of water for testing without providing further detail on their respective specification. The water was produced using Sartorius filtration system which was claimed to be comprised of reverse osmosis and ultra-filtration. There was no specification available for the water, and water was not tested regularly.

The issues raised from this section pertaining to microbiology laboratory have been satisfactorily addressed, and will be verified during future inspections.

2.8 Equipment, instruments and other devices

The laboratories generally had adequate types and number of equipment to perform the tests mandated. The SOP for carrying out preventive and corrective actions was reviewed which provided procedure for carrying out preventive and corrective actions. The procedure did not define various terms used such as corrective action, preventive action, and procedure and flowchart requires corrective action only.

An instruction manual for Atlas Copco (heatless adsorption compressed air dryers) was available which was used in isolator to supply compressed air. Maintenance of biosafety cabinet/BSC was done in-house for one of the BSC-II. The SOP for the operation and maintenance of the top-safe biosafety cabinet was referred to which provided procedure for calibration of BSC-II. The air velocity test and air sampling using settle plate were done every 6 month. From BSC record, it was found that anemometer was used without providing any detail on previous calibration and next calibration of velocity device.

The laboratory does not have GC.

2.9 Contracts

The SOP for the purchase of goods and services was available which described procedure for purchasing of various goods and services. It was noted that goods were purchased through the Government tender and purchasing guidelines whereas services were availed from the vendor without going through tender process.

It was also noted that NQCL did not subcontract any of the testing activities. An SOP for the subcontracting of tests was in place which provided provision of laboratory faces unforeseen circumstances e.g. workload, resources, need for further expertise etc. The procedure stated that chosen subcontractor shall be one that complies with the internationally accepted standards. If NQCL subcontracts any of the laboratories for testing, the laboratory shall be audited by NQCL. The laboratory should meet either ISO17025 or WHO Good Laboratory Practices requirement.

2.10 Reagents

The SOP for handling of chemical reagents was available which described procedure for handling of reagents. The SOP stated that records should be maintained for the preparation and standardization of volumetric solutions but it is noted that no record was maintained since almost one year. The reason being laboratory stopped following their SOP, and records were directly recorded on the analytical worksheets (AWS). The procedure also described storage duration of various types of reagents (buffers, acids, indicators, mobile phase and volumetric solutions) which was found to be contradictory to the current practice. The volumetric solutions were stored for duration of 1 month. The procedure also stated that standardization should be determined for any volumetric solutions more than a week old. Volumetric solutions, reagents and buffer were prepared as and when required by the analyst and recorded in respective analytical worksheets.

The issues raised from this section have been satisfactorily addressed, and will be verified during future inspections.

2.11 Reference substances and reference materials

The laboratory used primary reference standards which were procured from USP and International Pharmacopeia. It was noted that laboratory did not prepare in-

house/working standards. The working standards received from the manufacturers were used by the laboratory. The laboratory maintained a usage log of reference standards. A specific member of staff was designated responsible for the management of reference standards including receipt, registration, storage and issuance for use.

2.12 Calibration, verification of performance and qualification of equipment, instruments and other devices

A yearly maintenance schedule for all laboratory equipment/instruments was available wherein calibration/performance checks were divided into 12 months.

The issues raised from this section have been satisfactorily addressed, and will be verified during future inspections.

2.13 Traceability

The standards used were all traceable to the USPRS and the International Pharmacopoeia Standards.

The issues raised from this section have been satisfactorily addressed, and will be verified during future inspections.

2.14 Incoming samples

The receiving and registration of samples was managed by sample receiving officer. It was noted that laboratory receives request for the sample testing from the client and information pertaining to method of analysis, standards etc were provided by the laboratory before quotation was issued. Usually, samples were requested with reference standards, certificate of analysis, field analysis report etc. For molecules not in the pharmacopeia, the client needs to provide method of analysis. It was noted that Laboratory Information Management System (LIMS) was currently under development therefore hard bonded books were used for logging samples. The samples were assigned with NQCL number (or ID number) and same logbook was used to issue samples to analysts for testing purposes.

The samples were stored in sample store room under controlled temperature. The room had a data logger which was used to monitor temperature. The data was downloaded from the data logger once every month.

The samples were retained in sample retention room for a period of 6 month from the release of certificate of analysis (COA).

2.15 Analytical sheet

The standard analytical worksheets (AWS) were used in for all analyses for each sample. The AWS was reviewed. The certificate of analysis (COA) was comparable to WHO recommendation for COA content. The laboratory uses BP2012 instead of 2015.

The issues raised from this section have been satisfactorily addressed, and will be verified during future inspections.

2.16 Validation of analytical procedures

SOP for validation of methods of analysis was reviewed and noted that the procedure described validation of method of analysis to all pharmacopoeial and non-pharmacopoeial methods. It was noted that laboratory had never validated any of the methods. The laboratory also uses manufacturer' method but these were not verified by the laboratory before their use.

The issues raised from this section have been satisfactorily addressed, and will be verified during future inspections.

2.17 Testing

The sample receiving officer was responsible for issuing samples to analysts. It was however noted that laboratory did not maintain competency matrix which could ensure samples were assigned to analyst based on his/her training & competency of laboratory techniques.

2.18 Evaluation of results

The AWS were completed by the respective analysts and handed over for review by the respective reviewer from wet chemistry, instrumentation and microbiology laboratory. The analytical results were evaluated before certificate of analysis was finalised.

The SOP for handling of out of specification analysis results was available.

The issues raised from this section have been satisfactorily addressed, and will be verified during future inspections.

2.19 Certificate of analysis

Following analysis, the analyst responsible for the coordination of the sample prepared a report which was reviewed by a reviewer, and finally by the Director. The Director of NQCL was the authorised signatory.

2.20 Retained samples

The retained samples were retained for a period of 6 month before destruction.

2.21 Safety

Analysts were provided with protective clothing including safety glasses, protective facial mask, gloves, eye washer and emergency first aid box. Safety showers were installed in strategic areas of the laboratories.

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, **National Quality Control Laboratory (NQCL)**, **Nairobi, Kenya** was considered to be operating at an acceptable level of compliance with WHO Good Practices for Pharmaceutical Quality Control Laboratories.

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 laboratory, 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.