

**Prequalification of Medicines Programme
WHO PUBLIC INSPECTION REPORT (WHOPIR)
Quality Control Laboratory**

Part 1: General information

Name of QC Laboratory	Medicines Control Authority of Zimbabwe	
Physical address	106 Baines Avenue, PO Box 10559 Harare, Zimbabwe	
Date of inspection	20 - 21 January 2014	
Type of inspection	Initial	
Type(s) of testing included in the inspection	Physical and chemical testing	
Summary of the testing activities performed by the QC Laboratory	Type of Analysis	Finished products
	Physical/Chemical analysis	pH, water content, loss on drying, limit tests, dissolution, uniformity of dosage units (mass, content)
	Identification	HPLC (UV-Vis), UV-Vis spectrophotometry, basic tests
	Assay	HPLC, UV-Vis spectrophotometry, volumetric titrations

Part 2: Summary
General information about the company and site

The Medicines Control Authority of Zimbabwe (MCAZ) is a statutory body responsible for the regulation of medicines and allied substances in Zimbabwe. It was established by an Act of Parliament: The Medicines and Allied Substances Control Act No.1 of 1996 Chapter 15:03. MCAZ is the successor of the Drugs Control Council (DCC) and the Zimbabwe Regional Drugs Control Laboratory (ZRDCL). The Authority activities are:

- Evaluation and registration of medicines and allied substances
- Control of manufacture, distribution and storage of medicines
- Licensing of premises and persons
- Inspections and post-market surveillance
- Quality control testing of medicines and medical devices
- Administration of the dangerous Drugs Act on behalf of the Ministry of Health and Child Care
- Approval of medical devices

Chemistry Division consists of the Chemistry laboratory that performs chemical and physical tests to determine the quality of medicines and allied substances.

History of WHO and/or regulatory agency inspections

The laboratory expressed its interest in prequalification of their Chemistry Division on 28 January, 2013 and this was the first inspection performed by WHO inspection team within the Prequalification procedure.

The Chemistry Division had been accredited by the South African National Accreditation System (SANAS) for the HPLC and UV-Vis Techniques in the analysis of medicines. Laboratory was re-assessed by SANAS every year since year 2010.

Focus of the inspection

The inspection focussed on the WHO good practices for pharmaceutical quality control laboratories (GPPQCL).

Inspected Areas

The inspection covered the following sections of the WHO GPPQCL text

- Organization and management
- Quality management system
- Control of documentation
- Records
- Data-processing equipment
- Personnel
- Premises
- Equipment, instruments and other devices
- Contract
- 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

2.1. Organization and management

At the national level, Laboratory was legally authorized to perform the tests mentioned above. The Laboratory had managerial and technical personnel with the authority and resources needed to carry out their duties. The organization and management structure of the Laboratory was defined.

2.2 Quality system

The Quality Management System (QMS) was based on the ISO/IEC 17025:2005 requirements, other international standards and South African National Accreditation System (SANAS) requirements.

Quality Policy Manual was a high level general document covering the main activities and processes.

Quality Policy (QP) was part of the QMS. QP was affirmed in the Quality Policy statement from the Management.

Customer service: the main customers were:

- National Pharmaceutical Company (NATPHARM)
- Various donors who supply medicines via NATPHARM
- Ministry of Health and Child Care (MoHCC)

The Laboratory carried out various tests for post marketing surveillance and some tests for the Evaluations and Registration Division.

Management review (MR):

The SOP “Management reviews” was reviewed. Quality Management System Reviews were carried out quarterly. The Director General had the overall responsibility and chaired the meetings. The last QMS review was carried out on 17th September 2013. Draft minutes of the 21st QMS Review meeting, were presented to the inspector.

All previous QMS review minutes were available but not checked during the inspection.

Complaints:

The SOP “Complaints” was reviewed. Complaints should be investigated and CAPAs should be recorded and implementation checked by the Quality Manager (QM). CAPAs were reviewed and closed out by the Director General.

The new revision of the SOP was sent for the comments and checked by the inspector. According to the draft SOP the Director General would have overall responsibility of ensuring that all customer complaints were resolved.

Complaints were received from internal and external customers.

Internal audits:

The SOP “Internal QMS audits” was reviewed. QM and QMS internal auditors were responsible for overall implementation of the procedure. List of QMS internal auditors was presented to the inspector. According to the SOP QM should be deemed competent as an internal QMS auditor by the Director General based on relevant external training and experience. QM external training certificate issued by Corporate Quality Systems was presented to the inspector. Based on external training certificate Director General issued QM certificate of competency. QM external re-training was planned in 2014. QMS internal auditors were trained on site by QM on ISO 17025 Quality Auditing. QMS internal auditor’s certificates of competency were signed by Director General and were available for all auditors. QMS internal auditors were re-trained every 2 years – practical and theoretical training. Theoretical training effectiveness was assessed by open questions.

Audit findings and observations were recorded on the Audit Check list. Non-conformities raised during the audit were recorded on the Non-conformity report form. Audit report was forwarded to the QM within 10 working days of the date of audit. Root cause analysis and CAPAs should be recorded and undertaken within 30 working days from the audit date. Within 35 working days of audit date QMS internal auditors should follow up implementation of CAPAs.

Audits observations were classified as:

- Major
- Minor

Non-conforming (NC) work/Corrective and preventive actions (CAPA):

The SOP “CAPA procedure” was reviewed. SOP was very general and not detailed enough.

2.3 Control of documentation

The SOP “Document control” was reviewed. Controlled copies (hardcopies) of QMS were available for all employees. Soft copies of analytical templates were available for all analysts. The document distribution register for the QMS was available.

Control of the electronic documents:

Electronic documents were password protected, password to modify documents was known only by ICT and QM manager for the general QMS.

Regarding the documents (analytical worksheets) for the Chemistry Division, the Senior Analysts and the Head of Division (HoD) had password with read/write permissions and the analysts had read-only permissions.

Back up of electronic documents:

Master copies of approved electronic documents were stored on the QM’s computer with back-up on the local server and off-site server.

2.4 Records

Retention time for the different types of quality and laboratory records was defined as 5 years.

Records were kept in the documentation archive. Archive room ensured secure storage and retrieval of documents. Access to the archive room was restricted.

2.5 Data-processing equipment

The SOP “Procedure for Back-up” was reviewed. Data was stored on internal server. Replication of back-up data to the off site server was done automatically.

Draft revision of the SOP “Procedure for Back-up” was presented. According to the draft SOP back-ups should be done on weekly basis.

2.6 Personnel

The SOP “Staff Development and Training” was reviewed. The induction period was specified not less than 6 month. Afterwards competence assessment was carried out.

According to the SOP employees should undergo the following trainings:

- Safety issues
- Good Laboratory Practice
- Laboratory policies and procedures
- Standard test methods
- Instrumental techniques

Training

The SOP “Staff development and training” was reviewed. Senior analysts/Head of Division were responsible for analyst training. The procedure described three major areas for training, regarding technical in-house qualification, qualification using proficiency testing studies (PTS) results or intra-laboratory testing results and using historical data.

The SOP “Conducting Staff competence assessment” described criteria for assessing the effectiveness of training on a new analytical technique, based on internal PTS or using historical data.

Intra-laboratory proficiency test report was reviewed. Z-scores for five analysts were internally calculated and an evaluation of the obtained results was performed.

The “Staff competence list for 2014” for HPLC and UV-Vis was reviewed. This list was approved by the HoD in 2/1/2014.

Job descriptions:

The following job descriptions (responsibilities) were checked (form HRF08):

- Head of Department
- Senior Analyst
- Sample Reception Officer

Job descriptions seen were signed and approved.

2.7 Premises

The chemical laboratory facilities were recently upgraded and were acceptable in size and suitable for performing tests. Surfaces and finishing were suitable for easy maintenance. Premises were kept clean and tidy to ensure safe work. Temperature was routinely controlled and recorded in the different areas.

2.8 Equipment, instruments and other devices of chemical laboratory

Each item of equipment and instrument used for testing, verification and calibration was uniquely identified. Labels attached to the equipment and instruments showed calibration date, calibration due date and preventive maintenance due date.

It was noted that there were several equipments out of service, due to a delay on the calibration schedule related with the improvements done on the laboratory premises between December and January. A memorandum was sent to the Sample Reception Officer informing them that, due to the repair works in the laboratory, analysis would not be performed during this period of time.

All laboratory instruments and equipment had usage logbook and maintenance logbook.

2.9 Contracts

N/A

2.10 Reagents**Purchases**

Reagents were purchased from approved suppliers. The SOP “Purchasing services and supplies” was spot checked.

Evaluation of suppliers

Approved list of suppliers/vendors was presented to the inspector. List was authorized by QM. Suppliers list was updated annually.

Solvents and reagents

Reagents were stored in a separate room with other laboratory items.

Flammables were stored in an outside fireproof room.

After opening, buffers could be used for 3 months, organic solvents for 6 months, acids/bases 1 year and powders 2 years.

Water**Ultra purified water (HPLC grade water)**

Ultra purified water was sourced internally by Millipore equipment. Samples were collected from 2 sampling points. The following tests were carried on-line:

- Conductivity
- Resistivity

Other tests as per Eur.Ph. were carried out monthly.

Reagent solutions prepared in the laboratory

The inspectors did not see any reagent solutions prepared in the laboratory, as a consequence of the recent upgrade of the premises. However, the inspectors were informed that reagent solutions, as well as volumetric solutions, were prepared only when required for analysis.

2.11 Reference substances and reference materials

It was noted that the chemical reference substances were stored in suitable environmental conditions and were very well organized. The amount of each standard that was used for analysis was recorded on a Standard Logbook and it was fully traceable.

2.12 Calibration, validation and verification of equipment, instruments and other devices

Calibration, validation and verification of equipment's schedules for 2013 and for 2014 were shown to the inspectors, duly approved.

Each item of equipment and instrument used for testing, verification and/or calibration were uniquely identified, as well as the calibration status and the due date.

For all the inspected equipments, SOPs describing the internal verification were presented.

The calibration and verification data for the HPLC and UV-Vis equipment's were reviewed and found to be suitable.

Several calibration certificates were seen by the inspectors during the course of the audit, such as for balances and several thermo-hygrometers used for environmental monitoring.

2.13 Traceability

The reference material(s), equipment(s), reagent(s), analyst(s) and calculation(s) were suitably recorded in the analytical report and therefore traceability was deemed suitable and sufficient. It was seen by the inspectors that for tests performed before 2013 the traceability was not guaranteed, as there was no information on batches, references or internal codes of reagents and standards in logbooks and analytical worksheets. Changes were implemented during 2013 that guaranteed traceability at the present time.

2.14 Incoming samples

The Laboratory was not responsible for sampling. The Sample Reception Office received samples for all the organization.

Samples for testing were received from Licencing and Enforcement Division, Evaluations and Registration Division and Pharmacovigilance and Clinical Trials Division.

The SOP “Operating procedure for receipt and forwarding of samples” was reviewed. The SOP was applicable for all types of samples received at MCAZ.

The customer had to fill in the Sample Receipt Form. Every sample upon receipt was checked for integrity, appearance, labelling and storage conditions.

Each sample was uniquely identified with a MCAZ sample reference number and the samples were collected for analysis directly by the Chemistry Division.

Each customer identified which tests should be carried out and this information was forwarded to the division.

Sample registration was done manually. According to verbal statement Enterprise Resource Planning system would be introduced by the end of January 2014.

2.15 Analytical worksheet

Individual analytical worksheets (Excel) were developed and fully validated, for each test performed by the laboratory.

The SOP “Validation of Analytical Worksheets” was reviewed. The SOP described clearly how worksheets were elaborated and how the statistical validation was performed. It was recorded in a logbook for Validation of analytical templates.

The analyst’s logbooks were uniquely identified by the analyst code. The SOP “Logbooks” was reviewed and it contained a general description of the logbooks and was only applicable to analyst’s logbooks.

2.16 Validation of analytical procedures

Validation of analytical procedures in general was found to be in compliance with the OMCL guideline on “Validation of analytical procedures”.

Procedures for verification of HPLC methods and of UV-Vis methods were reviewed and found to be in line with the reference document.

2.17 Testing

During the inspection, no tests were performed in the laboratory.

Reporting of the results:

The SOP “Reporting of test reports” was reviewed. After analysis analysts wrote individual analytical reports for the tests carried out and then compiled the results in draft summary report. The sample file contained draft summary of results, individual reports and data obtained from instruments and remaining sample were submitted to the Senior Analysts for checking. Checking was done in accordance to the check list. Final checking was carried out by the Head of Division.

Specifications

The SOP “Handling of test items” was reviewed. It described that the test method should be followed as indicated by the customer in a specific form.

Investigation of Out-of-Specification results

The SOP “Handling of OOS results” was reviewed and found to be suitable.

Proficiency testing (PT)

The SOP “Inter-laboratory proficiency test” was reviewed.

PT plan for the Chemistry Division was presented to the inspector. The plan described tests on Identification, Assay, and Dissolution for the next five years. “Trend-analysis” report for all the PTs performed by the laboratory was presented to the inspector.

All the results, either satisfactory or not, were reported to the Laboratory Committee.

2.18 Evaluation of test results

The acceptance criteria for results were described in the SOP “Quality control of Analytical Techniques as well as in the several analytical worksheets for each test. The results obtained by each analyst were checked by a senior analyst or by the HoD.

Procedure on Reporting of test results was available and was found to be suitable.

2.19 Certificate of Analysis (CoA)

Draft CoA’s were generated by the analysts. CoA’s were checked by the HoD and approved by the Director General.

2.20 Retained samples

Post marketing surveillance samples were retained for 3 years or till the expiry date. Evaluation and registration samples were retained up to 5 years if required by Evaluations and Registration Division.

2.21 Safety

Safety and eye showers were seen to be available. Staff was wearing laboratory protective clothing.

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 **Medicines Control Authority of Zimbabwe**, located at 106 Baines Avenue, Harare, Zimbabwe was considered to be operating at an acceptable level of compliance with WHO Good Practices for Pharmaceutical Quality Control Laboratories for the scope activities listed below:

- Physical/Chemical analysis of finished pharmaceutical products and active pharmaceutical ingredients.

All the non-compliances observed during the inspection that were listed in the full report 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.