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Prequalification Unit Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Quality Control Laboratory

Part 1	**General information**
Inspected laboratory details	
Name of Laboratory	**Mission for Essential Drugs and Supplies (MEDS)**
Address of inspected laboratory site	Mombasa Road, opposite Nation Printing Press P.O. Box 78040 Viwandani, 00507 Nairobi, Kenya
Inspection details	
Dates of inspection	23-24 March 2023
Type of inspection	Follow up inspection
Introduction	
Brief description of testing activities	
General information about the laboratory	MEDS is a non-profit organization, located on the outskirts of Nairobi, Kenya. The organization was founded in 1986 and is registered as an ecumenical partnership for improving access to quality healthcare through the provision of essential medicines, medical supplies, and capacity

Type of analysis	***Finished products***	***Active pharmaceutical ingredients***
Physical/ Chemical analysis	pH, loss on drying, water content, refractometry, friability, disintegration, dissolution, density, uniformity of dosage unit (mass, content)	pH, loss on drying, water content, refractometry, density
Identification	HPLC (UV-VIS, DAD, RID, fluorescence detection), GC, UV-VIS and IR spectrophotometry, TLC, chemical reaction	HPLC (UV-VIS, DAD, RID, fluorescence detection), GC, UV-VIS and IR spectrophotometry, TLC, chemical reaction
Assay, impurities, and related substances	HPLC (UV-VIS, DAD, RID, fluorescence detection), UV-VIS spectrophotometry, GC, volumetric titrations, polarimetry, Determination of related substances/impurities and degradation products	HPLC (UV-VIS, DAD, RID, fluorescence detection), UV-VIS spectrophotometry, GC, volumetric titrations, polarimetry, Determination of related substances/impurities and degradation products

	building. The MEDS Quality Control Laboratory (QCL) became operational in 1997. The laboratory performs testing of Finished Pharmaceutical Products and Active Pharmaceutical Ingredients for Pharmaceutical Procurement Agencies, Pharmaceutical Manufacturers and Distributors, Regulatory Bodies and Donor Funded Programs. At the time of inspection, a new microbiological laboratory was under qualification, but it was not included in the scope of this inspection.
History	The laboratory was initially inspected by WHO PQ in March 2009. The last WHO PQ inspection was performed in April 2019. This was the 6th WHO PQ inspection The laboratory was also certified for ISO 9001:2015 and was in the process of being certified for ISO 17025:2017
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	The following areas and related documentation were inspected: - Organization and management - Quality Management - Data processing - Premises - Evaluation of test results, including investigation of OOS - Personnel – Training - Equipment – Calibration – Performance check - Traceability - Sample and material management - Supplier and contractors - Safety
Restrictions	N/A
Out of scope	The new microbiological laboratory was not covered.
Abbreviations	**Meaning**
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
CoA	Certificate of analysis
FPP	Finished pharmaceutical product
FTIR	Fourier transform infrared spectrophotometry or spectrophotometer
GMP	Good manufacturing practices
HPLC	High performance liquid chromatography (or high performance liquid chromatography equipment)
KF	Karl Fisher titration
LIMS	Laboratory information management system
MB	Microbiology
MR	Management review

NC	Non conformity
NCA	National control authority
NCL	National control laboratory
NRA	National regulatory agency
OOS	Out-of-specifications test result
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometry or spectrophotometer

Part 2	**Summary of the findings and comments (where applicable)**

1. Organization and Management

MEDS had a defined organizational and administrative structure. The organization was led by a Board of Trustees. The Head of Quality Services reported directly to the Managing Director.

The organization had procedures in place to ensure that its management and personnel were not subject to commercial, political, financial or any other pressure that might adversely affect the quality of their work. There was a policy in place to ensure the confidentiality of information.

2. Quality management system

An integrated quality manual describing the principles of the quality management system and defining the overall activities of MEDS was made available. The QM followed the ISO principles since the organization was certified for ISO 9001:2015 and the laboratory was in the process of being certified for ISO 17025:2017. The Quality Policy and quality objectives were adequately defined. Organization charts reflecting the reporting hierarchy were available and the laboratory activities were adequately described in SOPs and working instructions.

Management Review Meetings

Management review meetings followed the principles described in a written procedure. The management review meetings were conducted biannually. The agenda, the minutes, and the attendance register of the latest management review meeting held on 07.02.2023 (covering the period July to December 2022) were reviewed.

Data Integrity

A data integrity procedure was in place, and it referred to the principles of protecting and securing any data, information, records, and documents, in any form, from accidental or intentional unauthorized modification or destruction, through their lifecycle. The laboratory officer was responsible for reviewing audit trails for critical data to detect if they had been altered.

Internal audits

Internal audits were conducted in accordance with a written procedure. The Quality Assurance Manager was responsible for preparing the audit plan and determining the audit details (objective, audit areas, frequency of audit, auditors' independence), annually. The audit team comprised of a lead auditor and at least one audit team member and they had to be appropriately qualified. The internal audit schedules for 2022 and 2023 were reviewed. The records of the March 2023 internal audit were made available and included the internal audit report, the audit checklist, as well as the corrective action request for the observed deficiencies. The implementation and effectiveness of the CAPA plan were further monitored and assessed.

Deviations

A procedure for deviation handling was in place. Deviations could be classified as planned and unplanned deviations and further categorized as critical, major, or minor. The deviations were recorded in a register. Examples of deviations were reviewed.

Complaints

A procedure for dealing with client's feedback was presented. The Customer Services Officer was responsible for acknowledging the receipt of a complaint within 2 working days. Complaints were registered in the customer complaint register.

Trend analysis for complaints was performed annually. Examples of complaints' handled by the laboratory were reviewed.

Corrective and Preventive Actions

Identification, investigation, correction, and management of quality events were carried out in accordance with a written procedure which was applicable to the entire organization (corporate procedure). The non-conformities were categorized into critical, major, or minor and their handling was prioritized based on their criticality. The procedure adequately defined the process for identifying, implementing, monitoring, and assessing remedial actions.

Proficiency Testing (PT)

The laboratory participated in proficiency testing schemes on a regular basis. The PT for 2020, 2021 and 2022 were reviewed and found adequate

3. Control of documentation

A documentation system was established in accordance with a written procedure. The QMS documented information was reviewed periodically to ensure continued adequacy and suitability to meet set policies, objectives, and other requirements. The SOPs were uploaded to MEDS Intranet. The intranet could only be accessed by the local computer network and was password restricted.

The following working instructions and procedures were reviewed:

- Work Instructions for retained documented information disposal
- List of retained documented information disposal guidelines
- Control of retained documented information
- Retained documented information disposal guidelines

4. Records

Records of analytical testing were maintained, including raw data, calculations, method validations/ verifications, instrument use, calibrations and maintenance and sample receipt. Appropriate templates or electronic systems were used for registering the relevant data. In general, records were complete, signed and dated.

Logbooks for each equipment/instrument were available. Examples of laboratory equipment use logs were spot-checked.

5. Data processing equipment

Instruments such as HPLCs and IR were linked to workstations having the respective software. All raw data generated were stored as hard copies, as well as electronically in a server. Access to the instrument software was password protected. OpenLab CDS software was used for HPLC instruments. Audit trails were generated by the HPLC software and were verified as part of the data review process. Spreadsheets were designed by the IT-staff. All cells and formulas were locked, and data could only be entered in specific cells. Spreadsheets were stored on a server and were appropriately protected. Examples of spreadsheet calculations were reviewed.

6. Personnel

The laboratory had an adequate number of personnel with the necessary education, experience, and training to carry out the laboratory work. Responsibilities and duties were appropriately defined in written job descriptions. The job descriptions of Laboratory Analyst, Laboratory Manager, Laboratory Supervisor, and QA Manager were reviewed. A procedure for personnel training and competency assessment was presented. New employees had to undergo induction training. Training requirements were identified and documented based on staff positions and assigned duties. An employee assessment process was in place, and it included written evaluations, observation of a process, verification of response to situational problems, and testing of blind/known/already analysed QC samples. An annual training plan was drafted and monitored for implementation. The 2022 and 2023 training plans were reviewed and spot checks on training material and personnel evaluations were made.

7. Premises

The laboratory facilities were of suitable size, design, and construction. In general, the facilities were clean, tidy, adequately organized, and appropriate for the laboratory activities. Dedicated and independent rooms were available for received samples and retained samples. Additionally, separate rooms for storage of solid, toxic/hazardous, and volatile/flammable reagents were also available. Environmental conditions were monitored and controlled. Access to the laboratory facilities was restricted to designated personnel.

8. Equipment, instruments, and other devices

Generally, the laboratory had test equipment, instruments, and other devices for the performance of the tests and calibrations, validations, and verifications. Laboratory equipment was appropriately installed and maintained. Calibration status labels were attached to instruments. A list of equipment used in the laboratory was available in the LIF.

The following documentation was reviewed:

- Equipment Master List
- Maintenance Requirement List

- Master Equipment Maintenance and Calibration Schedule
- Water System Maintenance/Calibration Logbook
- Maintenance/Calibration of UV visible Spectrophotometer
- Maintenance/Calibration of Disintegration Apparatus
- Operation of Analytical Balance
- Qualification report of HPLC
- Operation of dissolution apparatus

9. Contracts

There was a procedure in place describing the principles of engagement with external providers of laboratory services. Before subcontracting any laboratory services, a review of quality documentation had to be performed including the accreditation of the external laboratory and the assessment of a completed questionnaire. Furthermore, an audit had to be carried out before drawing a contract for analytical services. Analytical reports and CoAs had to be reviewed before being accepted.

Suppliers were identified, evaluated, selected, and qualified in accordance with a written procedure. There were Work Instructions in place for supplier inspection. The selection of suppliers was performed every 5 years based on an invitation for expression of interest and screening of applicable documentation related to the product or service. A list of service providers was made available. Examples of audit reports of service providers were reviewed.

10. Reagents

Reagents were appropriately stored in different storage rooms (i.e., solid reagents, liquid/solvents, volatile/flammable reagents, and toxic/hazardous material). Storage conditions were monitored and controlled. Reagents' inventory was managed through LIMS (under qualification at the time of inspection).

11. Reference substances and reference materials

In general, Pharmacopoeial standards were used for the analyses. Reference standards were stored under the required conditions in the received samples storage area. An identification number was assigned to all reference standards and a person was responsible for their inventory. A logbook was used to register and monitor reference standards.

12. Calibration, verification of performance and qualification of equipment, instruments, and other devices

The laboratory had in place procedures for the maintenance, calibration, and qualification of laboratory instrumentation. A master list of laboratory equipment was available along with a maintenance requirement list. Please refer to section 8 for more information on the documents reviewed during the inspection.

13. Traceability

The laboratory had an adequate process in place to ensure traceability. Traceability of samples from receipt, throughout the stages of testing and the completion of test report was ensured and appropriately documented. Test results were traceable to analysts, analytical instruments, equipment, reagents, reference substances and test procedures.
Please refer to sections 18, 19 and 20 for more detailed information.

14. Incoming samples

The laboratory had a process in place for sample handling. The sample was submitted by the client along with an analysis request form. After visual inspection of the sample, a sample receipt checklist was completed, and a unique number was allocated to the sample which was recorded in a register as well as in an Excel file. The sample was stored in a storage room with restricted access prior to testing under controlled and monitored temperature (15-25ºC) and relative humidity (≤60%).

15. Analytical worksheet

The analysts recorded information on samples, performed testing procedures, calculations, and results in analytical worksheets.

The worksheets contained among others the following information:

- The test starting date
- Reference to specifications
- Identification of test equipment used
- Reference substances, reagents and solvents employed
- Interpretation of the results and the conclusion whether the sample was found to comply with the specifications

16. Validation of analytical procedures

There were Work Instructions in place for the validation of analytical methods. The procedure provided guidance on the extent of validation or verification needed. The laboratory performed testing based on pharmacopoeial and manufacturers' in-house methods, following appropriate method validation/verification.

There was also a procedure in place for analytical method transfer. Examples of analytical method transfer protocols and reports were reviewed.

17. Testing

Test procedures were adequately detailed and enabled analysts to perform the analyses in a reliable manner. Several analytical records and specific testing methods were reviewed in detail.

18. Evaluation of test results

Results were reviewed by qualified personnel for approval prior to the inclusion of results on the Certificate of Analysis. The results and compliance with the product specifications and analytical methods were checked and verified.

Work Instructions were in place describing the process of investigating OOS results. The Head of Quality Services was responsible for verifying/approving OOS results. The laboratory used a two-phase approach in the OOS investigation. The investigation of OOS results had to be completed within 30 days. A list of all the products with confirmed OOS results was presented. Any OOS result was recorded in an approved template. Invalidated OOS results were registered in a spreadsheet that was not part of the QMS documentation. The invalidated OOS results were handled through the deviation management system. Trending of confirmed OOS results was performed annually. The last trending report was reviewed. Several examples of OOS investigations were reviewed in detail

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

19. Certificate of analysis

Work Instructions for evaluating the test records, checking the analytical worksheets, drafting, reviewing, approving, and issuing the certificates of analysis were established. The Laboratory Manager was responsible for reviewing the laboratory records and certificates and the Head of Quality Services was responsible for approving the CoAs. The average turnaround time to issue a certificate of analysis was 25 working days from the date sample testing was completed.

20. Retained samples

The laboratory requested customers to provide a sufficient quantity of samples to ensure that a retained sample could be maintained. However, this was not always possible and the remaining quantities of samples after testing, retained in their original pack, were stored in a storage room with restricted access. Temperature and relative humidity were controlled and monitored.
Retained samples were maintained for one year after their expiry date

21. Safety

In general, the laboratory had in place appropriate safety measures. Laboratory personnel was appropriately gowned, and instructional gowning pictorials were posted on personnel entry. Safety goggles were worn by personnel performing analytical testing, where applicable. Emergency showers and eyewash stations were in place. Globally Harmonized System of Classification and Labelling of Chemicals (GHS) pictograms were posted in personnel entry and in storage areas.

Part 3	**Conclusion – Inspection outcome**

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, **Mission for Essential Drugs and Supplies (MEDS)**, located at **Mombasa Road, opposite Nation Printing Press, P.O. Box 78040, Viwandani, 00507 Nairobi, Kenya** was considered to be operating at an acceptable level of compliance with WHO GPPQCL 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.

Part 5	**List of WHO Guidelines referenced in the inspection report**

1. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1. ***Short name: WHO TRS No. 957, Annex 1***

2. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2. ***Short name: WHO TRS No. 961, Annex 2***

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.
Short name: WHO TRS No. 929, Annex 4

4. 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. ***Short name: WHO TRS No. 937, Annex 4***

5. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-First Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. ***Short name: WHO TRS No. 943, Annex 3***

6. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7. ***Short name: WHO TRS No. 961, Annex 7***

7. WHO Guidelines for preparing a laboratory information file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report. Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 2011), Annex 13. ***Short name: WHO TRS 961, Annex 13***

8. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 10. ***Short name: WHO TRS No. 1010, Annex 10***

9. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Forth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4. ***Short name: WHO TRS No. 1025, Annex 4***

10. WHO good manufacturing practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3. ***Short name: WHO TRS 1033, Annex 3***

11. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4. ***Short name: WHO TRS 1033, Annex 4***