

WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Quality Control Laboratory

Part 1: General information

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| Name of QC Laboratory | Laboratory of the Mission for Essential Drugs & Supplies (MEDS) | | |
| Physical address | Inside Zenith Steel Complex, opposite Mann Manufacturing Enterprise Road, Industrial Area Nairobi Kenya | | |
| Postal address | P.O. Box 78040 - 00507 Viwandani, Nairobi Kenya | | |
| Telephone number | +254 20 3920000 +254 20 551633/53/56 +254 20 2124453 | | |
| Fax number | +254 20 3920600 +254 20 556632 +254 20 556635 | | |
| Date of inspection | 3 - 4 February 2009 | | |
| Type of inspection | Prequalification inspection of a quality control laboratory | | |
| Type(s) of testing included in the inspection | Chemical, physical testing | | |
| Summary of the testing activities performed by the QC Laboratory | <i>Type of analysis</i> | <i>Finished products</i> | <i>Active pharmaceutical ingredients</i> |
| | Physical/Chemical analysis | pH, loss on drying, water content, conductivity, refractometry, friability, disintegration, dissolution, density, uniformity of dosage unit (mass, content) | pH, loss on drying, water content, conductivity, refractometry, density |
| | Identification | HPLC (UV-VIS detection), GC, UV-VIS spectrophotometry, TLC, chemical reaction | HPLC (UV-VIS detection), GC, UV-VIS spectrophotometry, TLC, chemical reaction |
| | Assay, impurities | HPLC (UV-VIS detection), | HPLC (UV-VIS |



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| | and related substances | GC, UV-VIS spectrophotometry, volumetric titrations, polarimetry Determination of related substances/impurities and degradation products | detection), GC, UV-VIS spectrophotometry, volumetric titrations, polarimetry Determination of related substances/impurities and degradation products |
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Part 2: Summary

General information about the company and site

Mission for Essential Drugs & Supplies (MEDS) is a registered trust of the ecumenical partnership of the Kenya Episcopal Conference (KEC) and the Christian Health Association of Kenya (CHAK). The organization was started in 1986 as an ecumenical partnership to improve accessibility to quality health care. The objectives of the organization are to provide a reliable supply of good quality essential drugs and medical supplies at affordable prices as well as to improve the quality of patient care through training in all aspects of health and general management with specific emphasis on the essential drugs concept and rational use of drugs.

Quality Control Laboratory of the Mission for Essential Drugs & Supplies (hereafter referred to as MEDS laboratory) started operation as an in-house laboratory in 1997 to test the quality of medicines procured and distributed by the organization. This was necessitated by:

- Liberalization of the Kenyan economy which opened the market to diverse sources of pharmaceuticals whose quality needed to be ascertained
- High costs and delays associated with sending samples to overseas laboratories

The laboratory plays a central role in the MEDS' Quality Assurance System by carrying out quality control function. This is aimed at ensuring that products distributed by the MEDS continuously meet international standards of quality. In addition, the laboratory also offers sample analysis services to external customers at a fee.

History of WHO and/or regulatory agency inspections

The MEDS laboratory had been pre-audited by WHO prequalification team on 27 July 2005 and 25-26 October 2006. The MEDS laboratory was not ISO 17025 certified and there were no audit or inspections performed by any regulatory authority.

Inspected Areas

The inspection focused on the quality management system and on conduct of , as the areas of quality control testing prequalified by the WHO.

The areas covered during inspection included the overall quality system to support the reliability and traceability of the result of the analysis. The areas of the WHO Good Practices for National Pharmaceutical Control Laboratories (GPCL) guidelines included the following items:

- Organization and personnel
- Quality management
- Personnel and training
- Premises and equipment
- Documentation and records
- Sample flow and sample storage
- Reagents and reference substances

- Traceability
- Safety

The following areas of quality control testing both for final products and active pharmaceutical ingredients were inspected:

- Identification using chromatographic methods (HPLC, GC, TLC) and spectrophotometric method (UV-VIS)
- Assays and determination of related substances/impurities using chromatographic methods (HPLC, GC), UV-VIS spectrophotometric method, volumetric titration and polarimetry
- Physical-chemical testing such as pH, loss on drying, water content, conductivity, refractometry, friability, disintegration and dissolution

2.1 Organization and management

The organizational structure of MEDS was described in an organization chart which was part of the Quality Manual. Responsibilities were specified according to the WHO Guide and laid down in individual Job Descriptions. The deputies of the key personnel were included in these documents.

The responsibilities in the job descriptions were not matching precisely the responsibilities in the Quality Manual; there was no reference in the job descriptions to the responsibilities defined in specific SOPs.

Personnel was experienced and qualified for their tasks. Since a new laboratory technician was hired there was one additional analyst available. The new analyst was still under training at the time of inspection.

2.2 Quality system

The Quality Assurance System of the MEDS laboratory covered the activities of the laboratory and was defined in a Quality Manual (QM). The QM included all the topics proposed in Chapter 2 of the WHO Guide. As a response to the last inspection Change Control and Deviation Control was included in the QM. The documentation system consisted of 4 levels defined in the QM: level 1: quality manual, level 2: procedures manual, level 3: work instructions and level 4: records.

2.3 Control of documentation

Control of documentation at MEDS laboratory was described in the standard operating procedure (SOP). All controlled copies of the quality systems documents were stamped “controlled”. Any document that was not valid but was retained for legal or knowledge preservation was stamped “obsolete” before storage.

There were two work instructions for the distribution and the amendment of documents in use. The distribution was documented on the distribution record sheet with the unique copy number, the name of the document, the name and signature of a person the document was distributed to. Changes or amendments to procedures were traceable from one version to the next.

2.4 Records

During the inspection records of training, receiving of samples, temperature control, analytical worksheets, reference substances, calibration and preventive maintenance and certificates of analysis, were reviewed. There were no records of method validations available as only compendial methods from the British Pharmacopoeia and United States Pharmacopoeia were used. Electronic data (chromatograms) were printed out and attached to the analytical worksheets. Certificates of analysis (CoAs) and other analysis reports were prepared by the Senior Laboratory Analyst and approved by the responsible person from the Quality Assurance or the Operations Manager. The laboratory ensured that the approval of the analytical worksheets was done in an appropriate way when the Senior Laboratory Analyst was performing the analysis.

The use of individual vials of reference standards, the source and the batch number of working standards, plan and the conclusion of self inspection and the handling of Out of Specification (OOS) results were recorded as a corrective action to the previous inspection in an appropriate way.

2.5 Data-processing equipment

There was no LIMS system in MEDS laboratory. For the HPLC systems and the respective Software, a validation file and a certificate of compliance from the manufacturer were available. Access to the system was password-controlled. The validation data of the software was not assessed by the inspectors.

The SOP Analytical data slightly differed from the OOS procedure.

2.6 Personnel

There were 5 staff members engaged in the laboratory. Head of Operations, Senior Operations Manager, Senior Laboratory Analyst and Laboratory Analyst were appropriately qualified, experienced and trained. A new analyst was under training.

The training system of the laboratory was revised as a corrective action to the previous inspection and was defined in SOP. The training requirements for new employees and existing staff were defined in appropriate detail and the documentation of the training was performed on specific controlled forms.

2.7 Premises

The laboratory premises were considered to be acceptable in size and suitable for storage and performing of the analyses. Monitoring of temperature and humidity was performed according to SOP. The minimum and maximum values for temperature were documented daily in a room specific log book. As a corrective action to the previous inspection the sample storage was separated from the archive of the documentation.

2.8 Equipment, instruments and other devices

Equipment and instruments used in the MEDS laboratory were listed in the Master Equipment List. The equipment was generally considered suitable for performing the intended analyses.

The personnel of the company were responsible for keeping track of the maintenance and calibration of the equipments and instruments.

Equipment including a polarimeter, pH-meters, UV/VIS spectrophotometer, HPLC, GC, balances, a titration processor and dissolution and disintegration test equipment were calibrated and maintained as appropriate and an individual logbook was kept on each instrument for these operations. The laboratory also kept a schedule for all necessary calibration, maintenance and qualification activities for critical equipment. Equipment which was not in use was labelled in an appropriate way.

See also 2.12 “Calibration, validation and verification of the equipment, instruments and other devices”.

2.9 Specifications

The MEDS laboratory maintained a specification archive consisting of pharmacopoeia and non-pharmacopoeia sources of specifications used for the testing. Mostly in use are the British Pharmacopoeia (BP) and the United States Pharmacopoeia (USP). On receiving the specification documents, the following details were recorded in the Master List of Documents of External Origin: the title of the document, version or date and the signature of the responsible person. The Senior Laboratory Analyst was responsible for maintaining the specifications archive and ensuring that older editions were replaced with the latest editions. The handling of specifications was defined in SOP Control of Documents.

2.10 Reagents

Laboratory analysts were responsible for the preparation of reagents. The procedures for preparation of reagents used for the different analyses were derived from the BP or the USP. The reagents used in the laboratory were labelled to indicate content, manufacturer, date received, shelf life and storage conditions. In-house prepared reagents indicated the date of preparation, name and initials of the responsible analyst and the date of expiry. Reagents were handled according to SOP.

Designated areas were used for the storage of hazardous material such as flammable substances, fuming and concentrated acids, bases and self-igniting materials.

2.11 Reference materials

In the MEDS laboratory mostly BP and USP reference standards were used which were maintained according to SOP.

There were Reference Materials Information files according to the WHO Guidelines available for both reference and working standards. As a corrective action to the previous inspection the use of the individual vials of primary standards was documented on a controlled form.

An identification number was assigned to every individual batch of reference material and was clearly marked on every container. According to SOP a new procedure was established for inspection of the validity of the working standards. Working standards were re-qualified annually by performing a full analysis. Results of re-qualification were documented on the Standard Validation form. There were no re-qualifications of working standards performed yet.

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

Handling, maintenance, calibration, and qualification of measuring equipment were performed according to SOP Management of Equipment and manufacturer's instruction manuals. Equipment including pH-meters, UV/VIS spectrophotometer, HPLC, GC, balances, a titration processor and dissolution and disintegration test equipment were found generally to be calibrated and maintained in an appropriate manner. Each item of equipment was uniquely identified. There were SOPs and manuals to explain the maintenance, calibration, and qualification frequency. Equipment that was malfunctioning or outside specified limits was taken out of service and tagged with an out of order label. There was a procedure in place for handling and documentation of out of calibration results.

There was no qualification documentation for Karl Fischer and the GC available during the inspection.

2.13 Traceability

The laboratory carried out various measurement procedures that fell into several categories including those for primary reference, routine measurement, semi-quantitative measurement and qualitative measurement. Primary reference materials used in the laboratory were procured from the USP, BP or WHO while secondary or working standards were standardized by comparison to the primary reference materials.

The analytical worksheets included the details of the used reference material, which were uniquely identified. Calibrations were performed either by the Kenyan Bureau of Standards or by the contracted external company – certificates stated the traceability to national and international standards of measurement. Analytical worksheets and calibration records contained information that demonstrated maintenance of the traceability chain.

2.14 Incoming samples

The sample flow was described in the Quality Manual. On receipt of samples a Test Request Form was filled in giving the following information: name of client, description of the sample, sample size, date received, manufacturing and expiry dates, tests required, sample storage requirements, name and signature of person requesting analysis and inspection findings.

All incoming samples and accompanying documents were assigned registration numbers. Separate numbers were assigned to requests referring different items, dosage forms or different batches. Each sample was issued with a registration number which was inscribed on each container. An Incoming Samples Register was used to record information on incoming samples including the registration number, date of receipt and the analyst to which the sample was assigned for analysis. The sample storage was monitored for temperature and humidity.

2.15 Analytical worksheet

QC testing was documented on analytical worksheets which content complied with the WHO guide. The issuance of analytical worksheets was performed according to SOP by the

Executive Secretary, who assigned an individual number to each worksheet issued to the analysts.

All the steps/individual pages of the particular analysis were signed by the person performing the work. The review of the data and calculations were performed by the Senior Laboratory Analyst and verified by signature in the end of the worksheet.

2.16 Testing

QC testing at the MEDS laboratory was mainly performed according to BP or USP. If there was no corresponding monograph in a pharmacopoeia the client was asked to provide MEDS with the respective specification and the methods of analysis. All the data were recorded in analytical worksheets (see above).

CoAs and analysis reports were prepared by the Senior Laboratory Analyst and approved by the responsible person from the Quality Assurance or the Operations Manager.

Recording the test results and the important details of the testing related to the traceability and the control of the worksheets have been discussed in more detail in other parts of this report.

2.17 Evaluation of test results

At MEDS laboratory the results of QC testing were reviewed and evaluated by the Senior Laboratory Analyst, who also may sometimes carry out the analysis himself. The review was documented by signature on the last page of the analytical worksheet.

The company had a procedure for the OOS situations.

2.18 Retained samples

Retained samples were kept in a separate retained sample storage area. In the retained sample storage area the temperature mapping was carried out. However it was not inspected during this inspection.

There was a SOP available for temperature or humidity monitoring.

2.19 Safety

There were protective clothes and devices (lab coats, gloves, safety glasses, fume hood and emergency shower) available in the MEDS laboratory. There was a system in place to have the safety data sheets available for each staff member and there were posters with safety instructions on the walls of the laboratory. Designated areas were used for the storage of hazardous material such as flammable substances, fuming and concentrated acids, bases and self-igniting materials.

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, the Laboratory of the Mission for Essential Drugs & Supplies (MEDS) was considered to be operating at an acceptable level of compliance with in compliance with WHO recommendations for Good Practices for National Pharmaceutical Control Laboratories.

All 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 laboratory, to a satisfactory level, prior to the publication of the WHOPIR.