World Health Organization

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Prequalification Team Inspection services
WHO INSPECTION REPORT
of the Quality Control laboratory

Part 1	**General information**		
Laboratory Details			
Name of the laboratory	M&L Laboratory Services - Bureau Veritas Group		
Address of inspected laboratory	40 Modulus Road, Ormonde Gauteng, RSA 2091 (Johannesburg) South Africa Tel. number: +27 (011) 661 7900		
Address of corporate office, telephone number and fax number	As mentioned above.		
Dates of inspection	18-20 October 2021		
Type of inspection	Routine		
Introduction			
Brief description of testing activities	*Type of analysis*	*Finished products*	*Active pharmaceutical ingredients*
	Physical/ Chemical analysis	pH, water content, loss on drying, water content (Karl Fisher), friability, disintegration, tablet hardness, dissolutions, viscosity, density, uniformity of dosage units	pH, water content, loss on drying, water content (Karl Fisher), melting point, conductivity
	Identification	IR, TLC, HPLC, UPLC, UV spectrophotometry and basic tests	IR, TLC, HPLC, UPLC, UV spectrophotometry and basic tests
	Assay, impurities and related substances	HPLC (UV, fluorescence, RI, conductivity, PDA) UPLC (PDA), GC, UV, potentiometric and volumetric titrations Determination of related substances/impurities and degradation products	HPLC (UV, fluorescence, RI, conductivity, PDA) UPLC (PDA), GC, UV, potentiometric and volumetric titrations

			Determination of related substances/impurities and degradation products

General information	M&L Laboratory Services is a contract testing laboratory based in Johannesburg, South Africa. The laboratory was opened in 1930 by two private individuals initially as a geochemical exploration laboratory. Over the years there have been many shareholders and the laboratory has expanded its scope of operations. It is currently a division of Bureau Veritas. Bureau Veritas is a global company with a variety of activities throughout 1500 offices and laboratories in 140 countries. However, M&L Laboratory was considered as an individual legal entity. M&L Laboratory Services comprised of 6 laboratories, i.e. Pharmaceutical, Microbiological, Food, Water, Agri and Pesticides laboratories. The Laboratory consisted of two sites; one based at 40 Modulus Road, Ormonde, Johannesburg, Gauteng and a Microbiological Laboratory located in Brackenfell Western Cape. M&L is a testing laboratory with no manufacturing activities performed either on this site or any another site. Only the Gauteng site was inspected during this visit.
History	The Laboratory was previously inspected by WHO-inspection team during December 2016. SANAS and SAHPRA (the national medicines regulatory authority) had audited M&L Laboratory. SANAS covered ISO 17025 requirements. The last SANAS inspection was on the 3-4 Nov 2020 and the respective certificate and schedule of accreditation was submitted. SAHPRA covered GMP requirements. The last SAHPRA inspection was conducted on the 1, 2 and 6 Mar 2018. A new license was issued in 2019. In addition, various local and international customers had audited M&L Laboratory e.g. Astra Zeneca, Novartis, Cipla and Pfizer.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Quality Management System Personnel Training and Safety Documentation and Records Premises and Equipment

	Validation – Qualification –Calibration Laboratory Practices Reference standards – Reagents - Water
Restrictions	Restrictions related to the COVID-19 pandemic had an impact on the laboratory activities, specifically related to the Laboratory's quality management and Microbiology laboratory inspection readiness. Poor electricity supply during the inspection was experienced.
Out of Scope	The Microbiology laboratory was excluded from the scope of inspection since the laboratory was not ready for an inspection. The stability activity was excluded from the scope of the inspection as the laboratory no longer stores samples for stability purposes. However, the respective testing was carried out upon request from clients.
Abbreviations	**Meaning**
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
CoA	Certificate of analysis
CAPA	Corrective action & Preventive action
DQ	Design qualification
FPP	Finished pharmaceutical product
FTIR	Fourier transform infrared spectrophotometry or spectrophotometer
GC	Gas chromatography or Gas chromatography equipment
GMP	Good manufacturing practices
HPLC	High-performance liquid chromatography (or high-performance liquid chromatography equipment)
IQ	Installation qualification
IR	Infrared spectrophotometry
KF	Karl Fisher titration
LIMS	Laboratory information management system
MB	Microbiology
MR	Management review
N	Normality
NC	Non-conformity
NCA	National control authority
NCL	National control laboratory
NRA	National regulatory agency
OOS	Out-of-specifications test result
OQ	Operation qualification
Ph.Eur.	European Pharmacopoeia
PM	Preventive maintenance

PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PT	Proficiency testing
PTS	Proficiency testing scheme
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QM	Quality manual
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
SOP	Standard operating procedure
TLC	Thin layer chromatography
TOC	Total organic carbon
URS	User requirements specifications
USP	United Stated Pharmacopoeia
UV	Ultraviolet-visible spectrophotometry or spectrophotometer
VMP	Validation master plan
VS	Volumetric solution

Part 2	**Summary of findings and recommendations**

1. Organization and management

The organization and management structure of the laboratory; including responsibility, authority and interrelationship of the personnel were specified in the organizational chart.. The laboratory was headed by Mr. Marc Roussel (Senior Vice President France and Africa) and Ms. Joanne Barton (Managing Director of M&L Laboratories) and comprised of the following Divisions:

- Pharmaceutical laboratory
- Quality assurance and QHSE
- Microbiology laboratory (Gauteng & Western Cape)
- Pesticides laboratory
- Water laboratory
- Food laboratory
- AGRI laboratory
- Administration
- Sales & Marketing

The laboratory had arrangements in their Quality Manual to ensure its management and personnel's impartiality to avoid pressures or conflicts of interest that might adversely affect the quality of their work. The laboratory had a policy in place to ensure the confidentiality of information contained in marketing authorizations and test reports.

2. Quality management system

The policies and guidelines concerning the assurance of the products tested were documented in the Quality Manual (QM). The Quality Manual encompassed elements of ISO 17025 and there were Standard Operating Procedures in place to cover the Laboratory activities. In addition, there were procedures in place to cover the requirements of the SAHPRA.

Management system documentation was established in the QM section 23.0, and consisted of

- Quality Policy and QM
- Quality procedures
- SOP
- Records

PT testing

SOP for Handling of proficiency test samples and control of out of specification proficiency test work was reviewed. The Laboratory was required to participate in inter-laboratory PT as per their policy.

Following Proficiency testing plan template was available:

Name of Method	**Method Number**	**Proficiency testing type (Proficiency testing, Inter-laboratory comparison; Intra-laboratory comparison**	**Name of PT scheme, names of participating laboratories where interlab comparisons are used,)**	**Frequency of participation/year or within the 2-year planned period**	**Number of samples tested per year using the method**	**Any problems experienced with participating in PT or evaluating PT results and taking corrective action**
Technique HPLC	Covered in PT scheme	PT Scheme	LGC Standards Pharmassure	Biannually	±10 000	None to date
Technique HPLC	Id and assay Method transfer validations	Inter Laboratory scheme/Customer	Numerous international Pharmaceutical testing facilities	As and when required by customer	±10 000	None to date
Aflatoxins HPLC	B, G, Total	PT Scheme	FAPAS/LGC	Biannually	±1 000	None to date

Internal audit

Internal audits were conducted as per the applicable SOP. Internal audits took place annually; either a vertical or witnessing audit was performed. Any non-conformances were addressed via Corrective Action procedure. Root cause analysis, corrective and preventative actions were defined in the procedure.

The Quality Assurance (QA) manager had overall responsibility and authority for the management of internal audits. Top management had responsibility to ensure that internal auditors were qualified by adequate training and that appropriate actions were implemented within agreed time intervals. Competency criteria of Internal auditors were specified in the SOP.

Internal audit schedule / review for 2021 and internal audit report "Pharmaceutical and Agricultural laboratory" related to the audit which took place on 15 Jun 2021, as well as the competency assessment of two internal auditors were randomly selected to verify the appropriateness of the applicable procedures.

SOP for Handling of deviations and the deviation register for 2021 were available and discussed. Deviations and the respective reporting route and timeframes were properly defined and classified in the SOP. Deviations were trended and discussed during the MR meetings.

Randomly selected deviations were reviewed to verify the implementation of the procedures. The deviations were successfully addressed and closed.

Complaints

SOP for Complaints and the customer complaint logbook for 2021 were available and discussed. Till the date of inspection, four complaints were registered, including pharma and microbiology laboratory. The procedure was applicable to external complaints.

The Laboratory Director / Quality Manager had overall responsibility for dealing with complaints. The process was illustrated in the SOP through the respective flowchart.

A complaint was selected to verify the implementation of the procedure.

Management Review (MR)

SOP for Management Review was available and discussed. MR was performed in accordance with ISO 17025:2017 standard, section 8.9. The SOP referred to annual management meetings and a standardized agenda was included in the SOP.

MR meetings should be attended by:

- M&L laboratory director
- Operational managers and supervisors
- Quality manager
- QA/QC coordinators
- Technical signatories
- HSE coordinator

The most recent MR meeting was held on 27 Nov 2020. The agenda, list of participants and the minutes of meeting, including KPIs used to assess the respective activities were reviewed. The recommendations for potential improvements were specified. The minutes of meeting was well organized and covered all the specific topics on the applicable agenda.

Change Control

SOP for Change Control (CC) and the CC register were available and discussed. The procedure was adequately described in the SOP.

This procedure was applicable to all corrective, preventive and continual improvement actions and to all changes that had an impact on any activity which might influence the Company's procedures, outputs and services. The SOP included, but was not limited to:

- Changes or modifications to major equipment and instruments
- Changes or modifications to computer programmes and software
- Changes or modifications to facilities and utilities
- Engineering changes
- Changes in storage conditions and PM programmes

CC register for pharmaceuticals / micro lab 2021 was available and discussed. A change control documentation was randomly selected to verify the proper implementation of the procedure.

Handling of deviation / non-conformities

SOP for Corrective and preventive actions and the respective register were available and discussed. The SOP found to be adequate. A follow-up was required to ensure that non-conformances would not be repeated, through an effectiveness assessment.

All non-conformances were trended by department as per ISO 17025 clauses. M&L director / Operational Managers should take immediate corrective and preventive actions when internal audit findings casted doubt of the effectiveness of the operations or on the correctness or validity of the test results.

Risk Management

SOP for Actions to address risks and opportunities was implemented. The procedures were established to offer a systematic approach for assessment, control, communication and review of risks to the quality of testing and associated results, and to cover continual improvement of the effectiveness of the QMS.

The steps to identify and assess any risk and opportunities were described in the SOP. A variety of risk management tools such as FMEA, FLOWCHARTS, HACCP, fault Tree analysis, and Fish bone were used and implemented in their procedures.

A risk registry was provided in pdf-format. Many risk assessments were done in 2019. Each risk assessment was assigned a number and a respective report was provided on a predefined template attached to the SOP. Risk no. 20/2019 was randomly selected and reviewed.

Deficiencies identified concerning the Quality Management system were adequately addressed in the respective CAPA plan.

3. Control of documentation

The laboratory established and maintained a system of procedures to control all documents (preparation, revision, distribution, return, archiving). A master procedure / document register identifying the current version status and distribution of documents was available in accordance with the applicable SOP. Each controlled document had a unique identifier, version number, date of implementation, reference to the previous version. The documents were released by the quality manager and authorized copies of documents were available at the point of use.

Document changes were performed as per SOP for Document and Data Control and Maintenance. Changes were evaluated, approved and documented in the document revision history prior to implementation. Relevant staff was trained on new and revised SOPs; the personnel acknowledged by signature that they were aware of applicable changes.

Laboratory workbooks and worksheets were issued by the Quality Department. Superseded documents were marked “Obsolete” and filed with the obsolete documentation. Superseded authorized copies were removed from use and shredded.

Procedures, Worksheets and Logbooks were compiled, reviewed, and controlled in accordance with SOP for Writing Standard Operating Procedures and Compiling Test Method Worksheets and SOP for Document and data control and maintenance.

4. Records

Applicable procedures were implemented through the following SOPs.

- SOP for Control of data and information,
- SOP for Management system documentation options,
- SOP for Technical records,
- SOP for control of management system documents,
- SOP for control of records.

Records were made of analytical tests, including calculation and derived data, method verifications, instrument use, calibrations and maintenance and sample receipt in logbooks containing consecutively numbered pages. The records were signed by analyst, reviewer and approver. Alterations were commented and references were made to appendices containing the relevant recordings, e.g. chromatograms and spectra. The specifications used were consistent with the information currently held in the dossier. Records were kept in an archiving room before being transferred to an external archiving facility on a monthly basis. Access to the archive was restricted to authorized personnel. The procedures for how to keep, retain and back-up the documentation was defined in the respective SOP. Computer back-up carried out at least weekly and the respective discs and/or backup tapes were stored at the external archiving facility. All documents generated should be stored for a period of six years. Technical records were controlled by QA / QC Co-ordinator or Laboratory Administrators using an applicable register/logbook whereby issue and return were signed for.

The history of randomly selected samples was checked (receipt log, storage conditions, tests, instruments and standards used, results, reporting, archive). For more details refer to section 18 of this report.

Deficiencies identified concerning Records have been adequately addressed in the respective CAPA plan.

5. Data processing equipment

An inventory of all computerised systems was available. Records on hardware configuration, installation and changes (incl. software updates) were required to be kept for computerised systems which were components of test equipment. Electronic data was protected from unauthorized access.

The following procedures were established to handle information stored in computerized systems:

- SOP for Archiving and retrieval of electronic data on empower,
- SOP for Data integrity,
- SOP for Empower administration. In this SOP, removing and disabling of the users and review of audit trails were described.
- The backup procedures were defined in the SOP for Procedure for maintenance of the Empower software system.

The Laboratory's backup procedures were defined as Hot Backup and Cold Backup. Hot Backup was performed automatically daily at 12 am through Monday to Saturday. External hard drive was also used for regular backup purposes and stored in the external block. The details of servers were indicated in the SOP for Data integrity.

Computer generated, time-stamped audit trails for electronic records were maintained on Empower software system and reviewed as part of the decision-making steps.

Spreadsheets (e.g. Excel®) were not used in the Laboratory. An electronic LIMS was deployed for sample management and issue of CoA.

Deficiencies identified concerning the Computerized systems have been adequately addressed in the respective CAPA plan.

6. Personnel

Due to the global pandemic related to COVID-19, the laboratory faced both organizational and personnel challenges across the workforce. Nevertheless, the Laboratory had managed to provide sufficient personnel with the necessary education, training, technical knowledge and experiences for their assigned functions to carry on the critical activities of Pharmaceutical laboratory.

All personnel involved in activities related to the quality and accuracy of testing were required to complete training. New staff members were required to work under supervision and were deemed competent by a senior staff member prior to commencing any analysis unsupervised. Ongoing competency was evaluated by validation of methods/equipment, participation in proficiency testing schemes; inter laboratory testing/method transfer activities. Training needs were identified by management. Training procedure was outlined in the applicable SOP. Execution of proficiency testing and review of training needs were also described in the SOP. Records were retained of all training and evaluations in personnel files.

Several attachments were provided to the SOP for training, to record the respective activities such as:

- A complete generic training matrix template
- Form for staff witnessing record template / competency assessment and
- Training assessment record template.

A folder was kept for each employee with documentation about the employee's job description, letter of confidentiality, letter of appointment, letter of deputation, training record, training program, competency assessment, list of competencies, CV, and certificate of qualifications and other training related documentation. The documentation for randomly selected employee was found to be satisfactory.

7. Premises

The facility consisted of three buildings; i.e. Building B, C & D. the pharmaceutical laboratory was in Building C. The facility was situated on a site which was approximately 4000 m². The pharmaceutical laboratory was divided into a preparation laboratory and an instrument room and was approximately 180 m². The pharmaceutical laboratory also had a unit for high risk testing laboratory. This laboratory was used for testing of antibiotic, oncology and hormonal drugs, testing scope of Penicillin, Cephalosporin, hormones, cytostatic/cytotoxic samples.

The laboratory facilities were of suitable size and design to suit the functions and to perform the operations to be conducted.

Separate storage facilities were maintained for storage of samples, retained samples, reagents, laboratory accessories and reference substances and if necessary, under refrigeration (2-8°C). The environmental conditions of storage rooms were monitored and controlled by digital data loggers. Adequate temperature mapping was regularly carried out and properly documented.

Gases were stored in a dedicated store, isolated from the main building. The laboratory provided separate fireproof room for storing flammable substances, fuming and concentrated acids and bases. The door was labelled with a certificate of fireproof. Access to the laboratory facilities was restricted to designated personnel.

Deficiencies identified concerning the Premises have been sufficiently addressed in the respective CAPA plan.

8. Equipment, instrument and other devices

The equipment, instruments and other devices used for the performance of tests, calibrations, validations and verifications were inspected to be verified whether they met relevant standard specifications. Generally, the equipment was regular qualified and/or calibrated.

Evaluation of measurement of uncertainty was described in the applicable procedure and predefined in the QM.

For more details, refer to section 12 of this report.

9. Contracts

Currently no tests were subcontracted for the pharmaceutical laboratory. Customers were advised if tests could not be performed by M&L.

The laboratory had a procedure in place for the selection and purchasing of services and suppliers in accordance with SOP for Externally provided products and services.

Contracts were signed and defined the contracted work and established duties and responsibilities for each party. The competence of the contracted organizations was periodically assessed, and records of these assessments were kept.

Prior to evaluation of suppliers, a supplier's desk top review template must be completed and approved. A checklist was completed by respective supplier to be categorized in critical, major or minor, based on the type of service to be provided. A list of suppliers/service providers with adequate information was retained and regularly updated.

Evaluation and audit documentation, as well as respective service agreements of selected service providers were reviewed and discussed.

10. Reagents

SOP for Standardized and non-standardized solutions was available and discussed. The procedure covered preparation, standardization and storage of volumetric solutions and preparation and storage of non-standardized solutions, reference standard solutions and reagents.

Solutions were prepared as stipulated in the latest editions of the relevant pharmacopeia's or supplied methods. Triple titration/determination was required to determine molarity. Volumetric solutions/reagents/mobile phase or solvents were labelled with information about Mobile Phase / solvent / solution, date prepared, expiry date, LRN (Laboratory Reference Number), analyst date and molarity (when applicable).

All volumetric solutions were checked on monthly basis, and when exceeded 6 months after the preparation date, they would be discarded. All reagents/solution were valid for 3 months from the date of preparation, unless otherwise mentioned. When expiry date was not indicated on the label or CoA, the chemicals were stored for 3 months. Standardized solutions were re-standardized every time before use.

Preparation of volumetric solution was verified to be traceable.

A Milli-Q water system was used to supply water to the laboratories. The water system was maintained and operated as per SOP for Procedure for the operation of the Milli Q system. pH, Conductivity, T.O.C (Total Organic Carbon) testing and temperature monitoring of the Milli-Q water was carried out daily. Chemical analysis of the water was carried out monthly and microbiological testing of Milli Q water was carried out weekly. The respective records were verified.

Deficiencies identified related to the water qualification have been adequately addressed in the respective CAPA plan.

11. Reference substances and reference materials

SOP for Procedure for reference standards in the Pharmaceutical Laboratory was available and discussed. Reference substances and reference materials (reference standards) were procured and supplied by the customer, mainly as USP or BP reference standards. On receipt, reference standards were labelled and stored as per storage requirements. Labels were color-coded for ease of reference e.g. reference standards that were to be stored in the fridge had a blue label. The certificate of analysis was stored with the register where usage was recorded as per the SOP. Reference standards were monitored for expiry dates and quantities and notification was sent to the customer within 3 months of the expiry dates or when a new order was required.

The storage and handling of chromatography columns were verified to be in accordance with the applicable requirements.

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

Each instrument was uniquely identified. Labels indicated the status of the calibration and the date when recalibration was due. Equipment underwent the necessary qualification, following a plan established by the laboratory. Balances were checked daily using internal calibration and regularly using suitable test weights. Requalification was performed annually using certified reference weights.

Records/logbooks were kept for items of equipment with information to identify the device, current location, and maintenance carried out. Use of the instrument was also recorded.

The following equipment was selected to verify the adequacy of performance verification / calibration / validation certificates. The respective SOPs for Operation, verification, as well as the respective logbooks were also reviewed:

- FT-IR spectrophotometer
- HPLC system
- Calibration certificate of the weights used for daily verification of balances
- Balances
- Hardness tester
- Karl Fischer titration
- Electrolab disintegration apparatus; i.e. Disintegration Unit
- pH Benchtop Meter with
- Electrolab tablet friabilator
- Hanson Vision Classic 6 Dissolution bath

Deficiencies identified concerning the Equipment and Devices have been adequately rectified in the respective CAPA plan.

13. Traceability

Test results were traceable, were appropriate, ultimately to primary reference substances.

All calibrations or qualification of instruments were traceable to certified reference materials and to SI units (metrological traceability).

14. Incoming samples

SOP for Procedure for samples receiving was established to define the process for the centralized receipt of samples, chain of custody, logging in of samples, safe handling, labelling, and storage of samples, within the M&L Laboratory Service. The samples were mainly tested for post importation purposes.

Pharmaceutical samples were stored on receipt in a locked sample room. Samples were allocated for testing and once testing was completed, samples were stored in the sample room labelled "Samples to be Returned" until either returned to the customer or sent off site for destruction.

Each sample submitted to the laboratory was tested in accordance with the customer test request which contained the following information:

- Description of the sample,
- Specification to be used for testing,
- Required storage conditions.

Samples, method, chromatography column with the respective register and reference standard register were accordingly assigned as a pack to the analyst by operational supervisors.

All delivered samples and accompanying documents were assigned a registration number. An electronic register was kept in which the required information was recorded.

Visual inspection of samples was carried out by the LIMS Order Entry Clerk or the LIMS Order Entry Co-ordinator to ensure that labelling conformed with the information contained in delivery documentation.

Deficiencies identified related to the Incoming and Retained samples have been correctly addressed in the respective CAPA plan.

15. Analytical worksheet

The analysts recorded information about samples, test procedures, calculations and results in analytical worksheets, which were completed by raw data. Full description of the test methods was added to the documentation.

The worksheets contained the following information:

- The date on which the analysis was started;
- Reference to specifications and, by which the sample were tested, including the limits; 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;
- Any deviation from the prescribed procedures, if applicable.

All values obtained from each test, including blank results, were entered on the analytical worksheet and all graphical data, whether obtained from recording instruments or plotted by hand, were attached or were traceable to the electronic record file or document where the data was available.

The completed analytical worksheets were signed by the responsible analyst and verified, approved and signed by the Lab manager. Independent reviews were also carried out. For corrections, the old information should be deleted by putting a single line through it; it should not be erased or made illegible. Alterations should be signed by the person making the corrections the date for the changes inserted. The reason for the change should also be given, when applicable.

Deficiencies identified related to the analytical worksheets have been adequately addressed in the respective CAPA plan.

16. Validation of analytical procedures

Analytical methods were provided by the customer. Method validation was performed by the customer at their facility. Method transfer was used to determine the ability of the laboratory to successfully perform the relevant analytical procedure. Method transfers were generally performed on new methods being transferred to the facility. SOP outlined the procedure for conducting method transfers at M&L Laboratory.

SOP for Analytical method validation was available and discussed. The validation criteria were implemented in a table as follows:

- For Customer method: No validation was required. Method transfer would be carried out.
- For Standard published method e.g. SANS, AOAC: a method verification was required
- For In-house developed method: a full validation was required
- For Pharmacopeial method e.g. BP, USP: method verification was required

A deficiency related to the Verification of analytical method has been sufficiently addressed.

17. Testing

The samples were tested in accordance with the work plan of the laboratory after completing the preliminary procedures.

Test procedures were described in detail and provided enough information to allow properly trained analysts to perform the analysis in a reliable manner. Where system suitability criteria were defined in the method, they were fulfilled.

18. Evaluation of test results and OOS investigation

SOP for Nonconforming work was in place describing the conduct of investigations of OOS test results. The SOP defined the requirements for handling nonconforming testing work within the Laboratory and described the investigations of OOS, OOT and OOE results. When a doubtful result (suspected OOS result) was identified, a review of the procedures applied during the testing process was undertaken by the supervisor and the analyst.

Doubtful results were rejected only if an error could clearly be identified.

In case the investigation was found to be inconclusive after Level 1a and Level 1b investigation, the SOP gave guidance on further instructions. The customer was notified and the instructions on the retesting plans (Level 2) would be communicated to the analyst by the operational supervisor / Departmental manager based on the instructions from the customer. Level 2 investigation covered all areas of the analytical testing and included hypothesis testing.

Once an error was identified, corrective and preventive measures were recorded and implemented. All individual results (all test data) with acceptance criterial was reported. The repeat of tests was done by a second analyst, at least as experienced and competent as the first one.

Analytical test reports were issued by the laboratory based on information recorded in analytical worksheets.

The test reports further included the following information:

- The background and the purpose of the testing;
- Reference to the specifications and methods used;
- The results of all tests performed (or numerical result with the SD of all tests performed);
- The statement whether the sample complies with the requirements.

Samples' documentation and their respective OOS investigations were randomly selected to verify the implementation of the applicable requirements and procedures.

Deficiencies were identified related to the OOS investigations have been adequately addressed in the respective CAPA plan.

19. Certificate of analysis

Results were reported on the Certificate of Analysis. Only approved personnel (technical signatories) could sign off COA's. Analytical reports were initiated by the analyst and reviewed by a supervisor / senior analyst.

A certificate of analysis was prepared for each sample/batch of a substance or product and contained series of information, among others:

- The results of the tests performed with the prescribed limits;
- A conclusion as to whether the sample was found to be within the limits of the specification;
- The date on which the tests were completed.

20. Retained samples

Refer to section 14 of this report.

21. Safety

Staff was wearing laboratory coats, including eye protection. Special care was taken in handling highly potent, infectious or volatile substances. Highly toxic and/or genotoxic samples were handled in safety cabinets. Safety showers were installed. Safety data sheets were available before testing was carried out.

All containers of chemicals should be fully labelled and include prominent warnings. First-aid kits were provided with adequate instructions. Staff were aware of methods for the safe disposal of unwanted corrosive or dangerous products. Warning signs were available throughout the laboratory.

Deficiencies related to the Safety have been adequately addressed in the respective CAPA plan.

Miscellaneous	
Assessment of the Laboratory Information File	Laboratory Information File was issued and provided in accordance with ISO/IEC 17025 SAHPRA / cGMP & WHO guideline.
Annexes attached	N/A

Part 3	Conclusion / Inspection outcome

Based on the areas inspected, the people met, and the documents reviewed, including the CAPA plan provided for the observations listed in the Inspection report ***M&L Laboratory Services - Bureau Veritas Group***, located at ***40 Modulus Road, Ormonde, Johannesburg 2091; South Africa*** is 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 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.

Part 4	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 GPPQCL Guidelines or ***TRS No. 957, Annex 1***
   http://www.who.int/medicines/publications/44threport/en/

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
   http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

3. WHO good manufacturing practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-sixth Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2.
   Short name: WHO TRS No. 970, Annex 2

   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/
4. 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
   http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

5. 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 No. 1033, Annex 4
https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations

6. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO GMP guidelines*** or ***TRS No. 986, Annex 2***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

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