World Health Organization

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WHO Prequalification Unit (PQT) - Inspection Services Team (INS)
WHO PUBLIC INSPECTION REPORT
of the Quality Control Laboratory
WHOPIR

Part 1	**General information**		
Laboratory Details			
Name of the Laboratory	Adcock Ingram Healthcare (Pty) Ltd – Research, Development & Implementation		
Address of the inspected Laboratory	1 Sabax Road, Aeroton Johannesburg, 2013 South Africa		
GPS Coordinates	Longitude: S 26.25753 Latitude: E 27.98105		
Address of corporate office, telephone number, and fax number	Same as above		
Dates of inspection	10 – 11 July 2025		
Type of inspection	Routine (follow-up) inspection		
Introduction			
Brief description of testing activities	*Type of analysis*	*Finished products*	*Active pharmaceutical ingredients*
	Physical analysis	pH, loss on drying, friability, disintegration, tablet hardness, uniformity of dosage units (mass, content), tablet dimensions, viscosity, density/specific gravity, redispersibility time, resuspendability, and sedimentation rate.	pH, loss on drying. Other tests are per pharmacopeial monograph or supplier method.
	Identification	(U) HPLC (UV-VIS, RI, DAD detection), GC (FID), TLC, UV/VIS spectrophotometry.	HPLC (UV-VIS, RI, DAD detection), GC (FID), TLC, UV/VIS spectrophotometry.
	Chemical Analysis: assay, impurities (includes degradants), related substances, dissolution rate,	(U)HPLC (UV-VIS, RI, DAD detection), GC (FID), UV-VIS spectrophotometry, volumetric titrations,	(U) HPLC (UV-VIS, RI, DAD detection), GC (FID), UV/VIS spectrophotometry, volumetric titrations, potentiometer.

	water content, residual solvents, limit tests	dissolution using USP I and USP II apparatus, potentiometer.	
	Stability studies	ICH conditions / WHO conditions	N/A
General information	The site was opened in April 2000 and is located in the light industrial area of Aeroton, Johannesburg. It has one immediate neighbor—Adcock Ingram Critical Care (Pty) Ltd., a sister company. Adcock Ingram Healthcare (Pty) Limited – Research and Development provides services to all Adcock Ingram manufacturing and corporate sites, including: • Adcock Ingram Healthcare (Pty) Limited – Wadeville (South Africa) • Adcock Ingram Healthcare (Pty) Limited – Clayville (South Africa) • Adcock Ingram Critical Care (Pty) Ltd – Critical Care (South Africa) • Adcock Ingram Healthcare (Pty) Limited – Bangalore (India) • Adcock Ingram Limited – Corporate (South Africa) **Activities Performed by the Analytical Laboratory** For Adcock Ingram Ltd. and Adcock Ingram Bangalore Pharma Private Ltd.: 1. **Quality Control and Product Release** o Final Product Release Certificate of products manufactured by Adcock Ingram sites (local and international) and licensed third-party contract manufacturers. 2. **Method Development and Validation** o Development and validation of analytical methods and related specifications for QC testing and cleaning validation. o Verification of analytical methods. o Transfer of validated methods to Adcock Ingram sites and third-party contract manufacturers. 3. **Product Testing and Investigations** o Testing of samples related to commercial product investigations, including customer complaints. o Analysis of development samples (laboratory and pilot-scale batches) for new and reformulated products. o Stability testing of pilot batches and selected commercial products. o Comparative in vitro dissolution studies for new and reformulated products. 4. **Stability** o Storage and management of pilot and commercial stability samples. 5. **Other Activities** o Participation in proficiency testing schemes. o Final Product Release Report for Adcock Ingram Limited products.	
History	The QCL was inspected by: - The World Health Organization on 13–15 October 2021 and 8–9 December 2016.		

	- The South African Health Products Regulatory Authority on 30 July–2 August 2019.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Organization and management, including: - Structure - QMS parameters - Documentation and records - Computerized systems Planning and strategic management, including: - Service providers and suppliers - Performance management - Proficiency testing & Improvements - Crisis Management Resources including: - Personnel - Premises - Equipment qualification - Reagents, reference substances Technical activities including - Handling of samples - Validation, verification and transfer of analytical methods - Testing, evaluation and reporting of results & OOS investigations Safety The Laboratory had established an e-portal for uploading documentation at the request of the inspectors. The documentation could be downloaded for review purposes before, during, and after the inspection.
Restrictions	N/A
Out of Scope	Refer to the report for each respective section.
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 Fischer 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
RS	Reference standards
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 system

1.1. Structural and general requirements

A detailed presentation of the laboratory was provided during the opening meeting.

The laboratory was legally authorized by SAHPRA to operate and be held accountable for test results, certificates of analysis, and related activities.

The senior manager was found to be responsible for establishing, implementing, and controlling the quality and data governance system, ensuring that appropriate policies, training, and technical systems were in place.

Procedures were established to prevent any influence that could compromise impartiality, including the declaration of conflict of interest and the maintenance of confidentiality for all laboratory information, such as marketing authorizations, analytical methods, and result/report transfers. The inspection team verified that contractors and consultants also signed declarations of conflict of interest and confidentiality agreements.

Organizational charts defined the laboratory's organizational and management structure, its position within the parent organization (Adcock Ingram Ltd.), and the relationships between management, technical operations, support services, and the QMS. The responsibility, authority, and interrelationships of all personnel who managed, performed, verified, reviewed, or approved work affecting laboratory results were specified in job descriptions.

Trained substitutes or deputies were nominated for key management and specialized scientific personnel. A staff member was designated as the quality manager, responsible for QMS compliance and granted direct access to the Head of Research & Development / Responsible Pharmacist. The Quality Manual provided some details on how internal communication was managed, including team meetings, verbal general announcements, and electronic communication.

1.2. Quality management system

The quality manager ensured that a QMS appropriate to the laboratory’s activities was established, implemented, and maintained. Prior to implementation, the QMS was communicated to and understood by relevant personnel, with all elements documented either electronically or on paper.

The quality manual included a quality policy, organizational structure, defined responsibilities, and a documentation framework. It also covered internal procedures, SOPs, personnel qualifications, and comprehensive policies addressing audits, CAPAs, complaints, management reviews, data governance, risk management, and service provider evaluations. SOPs for both administrative and technical operations were included, along with a reference to the validation master plan.

Observations related to the QMS were adequately addressed in the respective CAPA plan.

1.3. Control of documentation

A master list was established to identify the current versions and distribution status of documents.

Document control and review procedures ensured that each document included a unique identifier, version number, and implementation date. Authorized SOPs were accessible, regularly reviewed, and updated as necessary. Obsolete documents were replaced with revised, authorized versions, and previous versions were archived for traceability. Staff were trained on new and revised procedures. Documentation, including records, was retained for a minimum of five years in accordance with national legislation. Obsolete SOPs and WIs were retained for 6 years.

1.4. Change Control

The change control process implemented by the laboratory was supported by an SOP for Change Management. Changes were only implemented following management approval, with records maintained. Although the procedure included assessment of impact, gaps, risks, and opportunities, the effectiveness of its application remained to be demonstrated. The process was also stated to apply to software system changes.

The quality manager was responsible for ensuring that changes were documented, assessed, approved, planned, implemented, and reviewed. Subsequently, opportunities for improvement were identified in the procedures governing change control.

1.5. Control of Records

The applicable SOP described the issuance of controlled documentation, including logbooks, while a working instruction document addressed the filing and storage of documents. These procedures were limited to paper-based documents and records. The management of electronic records was addressed within the respective instrument SOP.

Traceability was ensured by documenting the name and lot number of the reference substance, including impurities used in the product analysis. The HPLC column serial number used was recorded in the test report. Additionally, a certificate of analysis for the reference substance was included as part of the test documentation. Calibration reports included the standards used for analytical balances and other devices.

All quality, technical, and scientific records were found to be legible, retrievable, and stored in a secure environment designed to prevent damage, deterioration, or loss.

Original records were kept under secure and confidential conditions, with access restricted to authorized personnel.

Quality management records included documentation from internal and external audits, inspections, management reviews, risk assessments, and corrective and preventive actions.

1.6. Control of Electronic Data / Computerized Systems

A list of computerized GxP systems was available, and provided pre-inspection:

A Validation Master Plan was prepared for the validation of computerized systems used for data collection, processing, recording, reporting, storage, or retrieval.

The Building Management System (BMS) was a controller- and software-based system used for monitoring Air Handling Units (AHUs) and maintaining specific environmental conditions in defined areas. The Data Acquisition System software allowed dynamic visualization of processes, with measurement values, alarms, and events displayed and stored. An upgrade of the system was in progress in accordance with the Change Control request dated 27 May 2025. The system was planned for upgrade. However, a deviation report had been raised, as it had been discovered that remote access

was not available, alarm notifications had not been set up, and data backups had not been performed. The deviation had been initiated on 20 Jun 2025, and it was still in process.

According to the VMP, periodic review was considered essential to maintain the validated status of equipment and computerized systems. This was performed by reviewing the history related to verification, calibration, repairs, and servicing of the instrument's or equipment's critical parameters related to its functionality, as well as the associated procedures. The results of the review were documented in a Validation Review Report, which concluded either that the validation status was upheld or that revalidation was required. If requalification or revalidation was deemed necessary, the decision was justified and documented through the change control process.

A logbook was available for the annual check of access rights for each software system (user registers) to verify the users and their access levels.

Retirement of validated equipment was controlled as per the applicable SOP.

Selected documentation was reviewed for the operating system for GC and HPLCs in the laboratory.

A digital platform was used to raise and track deviations, change controls, and CAPAs.

The procedure for the creation and operation of Excel spreadsheets described the validation of Excel spreadsheets. An appropriate description of the security measures for Excel spreadsheets was provided.

Computerized systems were protected from unauthorized access, tampering, and loss. It was verified that the chromatography system was capable of recording system failures and that appropriate actions were taken by the laboratory.

For test data in computerized systems:
- Electronic data were protected from unauthorized access, with an audit trail enabled and periodically reviewed.
- The inspected computers and automated equipment were generally maintained properly and provided with the necessary environmental and operational conditions to ensure data integrity, with one exception (refer to observations for details).
- Electronic data were, in general, backed up at regular intervals, were retrievable, and were stored appropriately to prevent data loss, in accordance with SOP for Data backup and retention, issued 31 January 2025. The procedure covered all servers for daily, weekly, monthly, and yearly backups, with pharmacovigilance data retained for at least ten years post-registration. Integrity checks were performed using applicable tools, with daily reporting and replication from the respective site to a disaster recovery site. Backup failures were logged, investigated, and corrected, with annual disaster recovery testing in place. The SOP for Data backup's content was presented in structured text format, outlining responsibilities, technologies used, backup schedules, verification, disaster recovery, and procedures.

The Laboratory did not use an electronic LIMS.

1.7. Corrective and preventive actions

The CAPA process was managed in accordance with the respective SOP. This procedure applied to CAPAs triggered by change controls, OOS, OOT, inspections and audits, and complaints. Any deviation or nonconformity reported by staff or otherwise identified was investigated through root cause analysis, as outlined in the applicable SOP.

The laboratory identified responsible persons for required actions and established timelines for their implementation. The effectiveness of corrective actions taken was reviewed. A report documenting deviations, root causes, corrective actions, and their outcomes was prepared, recorded, and retained. Deviations and nonconformities, their impact on the management system, and related risks and opportunities were regularly analyzed.

Any situation potentially leading to a deviation or nonconformity was addressed appropriately, resulting in preventive actions. Depending on their potential impact, preventive actions were treated as either risks or opportunities.

1.8. Internal audits

The Quality Assurance department was responsible for organizing internal audits, including planning, establishing, implementing, and maintaining an audit program that could be adjusted based on risk. This was managed in accordance with the respective SOP, which included the necessary provisions for conducting internal audits:

- Planning and performing audits periodically by the quality manager (at least once a year) to enable systematic assessments.
- Defining the scope of each audit using risk-based criteria, including critical activities and implementation of corrective and preventive actions.
- Ensuring audits were conducted by trained personnel.
- Reporting audit results to relevant management and discussing them during management review.
- Implementing appropriate corrections and corrective actions promptly upon identifying nonconformities.
- Monitoring the effectiveness of implemented corrective actions.
- Retaining records as evidence of the audit program implementation and results.

Records of the April and June 2025 audits of the QA and analytical laboratories, respectively, were reviewed.

1.9. Complaints

This was out of scope given that the site was not receiving complaints from external clients.

1.10. Management Review

Management Reviews were carried out in accordance with the respective SOP. Laboratory management reviews were convened biannually, at planned intervals, and at least annually, to monitor the effectiveness of the management system.

Senior management, including the responsible management board director, laboratory director (or equivalent), and quality manager, ensured that previous decisions had the intended impact on laboratory activities and resources. Planning for the subsequent period was undertaken to maintain the suitability, adequacy, and effectiveness of the laboratory QMS.

Outcomes of management reviews were recorded, documenting all decisions and actions related to the effectiveness of the QMS, improvement of laboratory activities, availability of required resources, and necessary enhancements.
Records of management reviews included, but were not limited to, information on:

- Performance management.
- Status of actions from previous reviews.
- Changes in internal and external factors impacting the laboratory.
- Results of internal and external audits or inspections and any required follow-up actions.
- Changes in laboratory activities.
- Adequacy of resources.
- Corrective and preventive actions.
- Effectiveness of implemented improvements.
- Trend analysis results.
- Atypical and OOS results.

1.11. Improvement

Participation in proficiency testing was conducted in accordance with the applicable SOP. The schedules for 2024 and 2025 were available and reviewed. A separate schedule was prepared for each year. All tests were reported to have been passed satisfactorily.

2. Planning and strategic management

2.1. Externally-provided services and supplies

The qualification and management of laboratory vendors and service providers were performed in accordance with established procedures. The respective SOP governed the management of vendors of laboratory consumables, while another SOP outlined the management of service providers for laboratory equipment.

A register of equipment service providers and a separate register of lab consumables suppliers were available and maintained. Certification records for lab consumables were retained and available.

A list of approved laboratories was also available and reviewed. The documentation demonstrated that supplier and service provider qualification and monitoring processes were implemented as per procedural requirements.

These SOPs were submitted to the inspection team after the inspection due to time constraints, and no supporting documentation could be reviewed during the inspection.

2.2. Review of tenders and contracts

This topic was not inspected during the current inspection. No discrepancies had been identified in this area during the previous inspection.

2.3. Performance Management
Refer to Section 1, Organization and Management.

2.4. Quality Risk Management
This topic was not inspected during the current inspection.

2.5. Crisis Management
A Crisis Management and Business Continuity framework was established and implemented for the laboratory as outlined in the Business Continuity Plan (September 2024) and the respective SOP. These procedures were designed to ensure a structured and effective response in the event of emergencies such as power failure, water outage, equipment breakdown, flooding, natural disasters, or other disruptions affecting laboratory operations.

Key elements of the crisis management included the identification of critical business functions, defined roles and responsibilities, emergency evacuation procedures, activation of a Business Continuity Plan, and coordination with alternate sites or external laboratories. Recovery measures involved relocation of personnel, the use of standby systems (e.g., generators, UPS, backup water tanks), and outsourcing of testing when necessary. Communication protocols were also established for both internal and external stakeholders. The process aimed to ensure safety, minimize operational disruptions, and maintain regulatory compliance during crises.

These SOPs were provided after the inspection due to time constraints; therefore, the effectiveness in practice could not be inspected.

2.6. Communication management
Refer to Section 1.1: Structural and General Requirements.

3. Resources

3.1. Personnel
Personnel with the necessary education, training, technical knowledge, and experience for their assigned functions were employed either on a permanent or contractual basis. Procedures and criteria for assessing personnel competence were established in accordance with the QMS.

Staff undergoing training were appropriately supervised, and their performance was assessed upon completion. These assessments were fully documented.

Specific laboratory activities were authorized by the laboratory director or a designated person, ensuring that only qualified and trained personnel were permitted to perform them.

Procedures and criteria for the continuous assessment of personnel competence were documented, and training or requalification was provided as appropriate. A matrix of analyst competencies, along with documented procedures and assessment criteria, was maintained. It was noted that this system was limited to analysts and had not been extended to other functions, such as the QA department.

Results of evaluations upon successful completion of training were recorded and made available. The training and qualification of analysts were conducted in accordance with the respective procedure, which applied to both new and existing employees. Requalification was required every two years or in cases of frequent OOS results or major changes.

The level of competency for each analyst was documented in 25/QA/007 and categorized as either standard (perform) or advanced (perform and review).

Observations related to Personnel (Resources) were adequately addressed in the respective CAPA plan.

3.2. Premises

The laboratory layout was documented in the LIF and SMF. The facility was of suitable size, construction, and location to support pharmaceutical testing activities.

The premises adequately accommodated the necessary features of a pharmaceutical testing laboratory and minimized risks to staff health and the quality of analytical results. Emergency exits were available.

Designated entrance and sample reception areas were provided for staff, visitors, and samples. Rest and refreshment rooms, as well as toilets, were located separately from laboratory areas.

Storage facilities were appropriately organized to ensure the correct storage of samples, reagents, and equipment. Safety procedures were rigorously implemented for the handling of toxic or flammable reagents.

The laboratory was equipped with adequate instruments and equipment, including workbenches, workstations, and fume hoods. Separate instrument rooms were available for different measurement techniques, as required. Safety equipment was adequately provided and appropriately located. Measures were in place to ensure good housekeeping and regular cleaning routines.

Archive facilities were provided to ensure the secure storage and retrieval of documents. Paper records were kept in secure rooms, while electronic records were retained with duplicate copies at an external facility managed by the corporate IT unit.

Environmental conditions, including lighting, energy sources, temperature, humidity, and air pressure, were generally appropriate for the functions performed. These conditions were monitored, controlled, and documented in general.

Observations related to Premises (Resources) were adequately addressed in the respective CAPA plan.

3.3. Equipment, instruments, and other devices

The laboratory was required to have the necessary apparatus, equipment, instruments, or instrument systems used in pharmacopeial analyses to ensure the correct performance of tests and related activities.

All equipment, modules, and accessories were uniquely identified, including manufacturer details, identification numbers, location, and equipment specifications.

The documentation of selected equipment was reviewed to verify whether analytical equipment was adequately qualified, or the periodic performance checks were properly carried out.

The HPLC column used for a randomly selected identification test was reviewed. A logbook for column usage was available for each column, documenting the analyst, product, notebook reference number, mobile phase, and any relevant comments. An SOP was available, outlining the receipt, handling, storage, ordering, and maintenance of HPLC, UPLC, and GC columns. The verification of a randomly selected column was requested to be reviewed.

A preventive maintenance schedule and equipment qualification (EQ) plan were established for analytical equipment. Preventive maintenance activities were performed either by the laboratory or by a competent external service provider.

All calibrations and equipment qualifications were traceable to appropriate references, and any changes to analytical equipment were required to follow a formal change control process.

Equipment logbooks were maintained to document the complete equipment history, including records of maintenance, calibration, and qualification.

Observations related to the Equipment were adequately addressed in the respective CAPA plan .

3.4. Reagents and materials

Reagents and chemicals, including solvents and materials used in tests, were required to meet appropriate quality standards and be suitable for their intended use. Reagents were to be obtained from verified and approved qualified providers and accompanied by certificates of analysis and material safety data sheets.

Regular verification of water quality and appropriate storage conditions for reagents were required to ensure continued suitability for use.

3.5. Reference substances

Reference and working standards were managed in accordance with the respective SOP. Working standards were prepared by the laboratory upon receipt of the substance from the manufacturer, accompanied by the respective documentation, and qualified according to the applicable qualification method. A certificate of analysis was issued accordingly.

Reference substances were obtained from reputable commercial sources or were supplied by the pharmaceutical product manufacturer.

The control, receipt, and consumption of reference substances and materials were overseen by a designated staff member and documented in a logbook. An Excel spreadsheet was also maintained to

provide an overview. The register was kept for all reference substances and materials, containing detailed information including identification number, description, source, receipt date, batch designation, intended use, storage location, expiry or retest date, certificates of analysis, and material safety data sheets.

All reference substances and materials, excluding pharmacopeial reference substances, were assigned an identification number. Each batch received a new identification number, which was marked on individual vials and referenced in the analytical worksheets.

Before use, the intended use and expiry or retest date of reference substances were confirmed, and the corresponding information was included in the test reports.

The CoA for Ascorbic Acid WS, the corresponding laboratory notebook, and the Register for WS issuance and usage were available and discussed.

4. Technical activities

The laboratory was not involved in any sampling activities. Sampling was the responsibility of the distributors. The laboratory was, at the time of inspection, responsible only for the analysis of products on behalf of the MAH, Adcock Ingram, and for post-importation samples.

4.1. Incoming samples

The laboratory provided an electronic list of tested samples covering the period from 2023 to 2025 prior to the inspection. Manual registers were maintained for the period from October 2021 to December 2022 and were available for review. All samples analyzed were post-importation products, with testing limited to Identification and Assay. The analytical methods used were primarily based on the respective manufacturers' methods, supplemented by in-house developed and validated procedures, where necessary.

The laboratory had not performed any analysis for WHO products, as only one request had recently been received.

Samples submitted to the laboratory were managed in accordance with SOPs for Post Import Release of Products Intended for Sale, for Sample Management, and for Sample Management for WHO, UN & Other.

A standard test request form was not completed for every sample submitted to the laboratory, as the products were received from Adcock sites with the prior understanding that only Assay and Identification of the active substances were to be performed.

The sample registration log and the sample transfer form included the following details:
- Name and date of receipt of the provider.
- Material source.
- Sampling date.
- Expiry date.
- Quantity.

- Data logger ID.
- Name of supplier.

Before commencing testing, the laboratory was required to review the test request to ensure the following:
- A sufficient number of product units were provided for post-importation products, as established by QA, with the warehouse responsible for ensuring availability.
- The laboratory possessed the necessary capability and resources to conduct the required tests.
- The available tests or methods were suitable to meet customer requirements.
- Any issues identified during the review were to be resolved with the request originator prior to initiating testing, and a record of the review was to be retained. If the laboratory determined which samples to test, the test request form was required to be adjusted accordingly.

Each sample and its accompanying documentation were assigned a unique registration number in chronological order, documented in a logbook. The register recorded the sample registration number and the date of receipt. Samples were segregated on labelled shelves into three groups:
- Awaiting testing
- Post-importation retention quarantine
- Retained samples.

Verbal requests for analysis were accepted only in emergencies and in very rare cases, with all relevant details promptly documented until written confirmation was received.

All documentation accompanying each numbered sample sent to the specific unit was required to include the correct identification number, origin, purpose, and any additional information necessary for receipt and testing activities.

Observations related to Incoming samples were adequately addressed in the respective CAPA plan.

4.2. Selection, validation, and verification of analytical procedures

Analytical procedures to be used for testing—whether for compliance or investigative purposes—were selected by the laboratory prior to the start of the analysis.

All analytical procedures employed were ensured to be suitable for their intended use.

The laboratory either used validated methods received from the licensing partners and verified them or performed method validation for products manufactured by Adcock manufacturing sites.

4.3. Technical records

The laboratory notebook was a paper based internal document used by analysts to record information related to the sample, test procedures, reagents, standards, materials, calculations, and test results. Once a sample was received and logged in the respective logbook, a laboratory notebook was issued by the sample custodian. The custodian completed the book number, product name, lot numbers, and issuance details, including signature and date. This process ensured that laboratory notebooks were issued only under the supervision of the QA department.

The notebook included all raw data obtained during analysis. The notebook served as documentary evidence to confirm whether the sample met the required specifications or to support an OOS result. A unique laboratory notebook / analytical worksheet was used for each numbered sample or group of samples. Completed analytical worksheets from different units relating to the same sample were combined to form a complete record.

The analytical worksheet included the following information:
- Registration number of the sample
- Page numbering, including the total number of pages (including annexes)
- Date of the test request
- Dates at which the analysis was started and completed
- Name and signature of the analyst
- Description of the sample received
- References to the specifications and a full description of the test methods used, including applicable limits, or a traceable reference to the method
- Identification of the test equipment used
- Reference substances used, including provider, lot number, potency or content
- Results of the system suitability test, if applicable, and any analytical acceptance criteria
- Identification of reagents, solvents, and columns used, if applicable
- Results obtained, including those from other internal sections or external laboratories, if applicable
- Interpretation of results and conclusions, including compliance with specifications, approved and signed by designated qualified personnel
- Further comments, such as deviations from prescribed procedures, approval and documentation of nonconforming work, or details on transfer of the sample to another unit or contract laboratory, including transfer and result dates
- All values obtained from each test, including blank results, were immediately entered on the analytical worksheet. All graphical data, whether obtained from recording instruments or plotted by hand, were attached or traceable to an electronic record or document.

The completed analytical records were signed by the responsible analyst and reviewed and approved by designated qualified personnel, either in paper format or electronically. Calculations and data transfers were checked appropriately and systematically.

Any changes made to original records, either in paper or electronic format, were traceable to what was changed, who was responsible, when it was performed, and why. The deletion of data was not acceptable. When a mistake was made in an analytical worksheet or when data or text needed to be amended, the correction was traceable.

The analytical worksheet and any attachments, including calculations and recordings of instrumental analyses, were archived together with the specification.

4.4. Testing

Testing methods were made available by the medicine licensing authority when testing for compliance with the specification. The methods were either validated by the manufacturer or validated by the laboratory specifically for the Post Importation Release specification. The laboratory was responsible for the release of products related to post-importation.

Test procedures were described in detail and provided sufficient information to allow trained analysts to perform the analysis in a reliable and reproducible manner. As a result, the process of solution preparation was not separately recorded in the analytical worksheets. Instead, the worksheets included information on the equipment and materials used, along with the weighing slips and calculations. System suitability criteria defined in the method were fulfilled. The laboratory also operated in accordance with SOP for Weight Agreement and System Drift, effective 15 August 2023, for system suitability (if not mentioned in the test method).

The sequence of injections was performed in accordance with SOP for Chromatographic Integration, issued 31 August 2023. The specific limits and acceptable ranges were defined in the respective analytical methods. For peak integration, only "Baseline to Baseline" integration was permitted. Manual integration was not allowed, and the function was disabled in the chromatography system, as verified during the inspection.

System checks using standard solutions were conducted prior to each analytical run to ensure system stability. In case of any failure—referred to as analytical anomalies—the applicable SOP was followed to document and evaluate the issue in a dedicated logbook, i.e., the Register of Analytical Anomalies. Instrument failures were also reflected in the system audit trail. More serious failures were additionally recorded in the respective maintenance logbook, while minor actions, such as refilling gas, were not documented. It was recommended that all failures occurring during an analytical run be consistently recorded.

A sample was randomly selected for review of its respective documentation, covering the entire process from receipt of the sample to the issuance of the CoA, including sample retention. Where applicable, the investigation of any OOS results was also reviewed.

4.5. Evaluation of test results

For compliance testing, the product was required to meet all acceptance criteria defined in the approved specification. Test results were compared with the specified limits to determine whether the sample met the requirements, and a conclusion was drawn regarding conformity with the specification.

Each test result was traceable to a suitable primary reference substance, either from a pharmacopoeia or the manufacturer.

Test results were reviewed and approved or rejected by designated qualified personnel, in accordance with the competency matrix.

4.6. Measurement uncertainty

This area was not inspected. It will be reviewed during the next inspection, following the laboratory's completion of a gap analysis to ensure that its practices are aligned with the newly revised WHO guideline for pharmaceutical quality control laboratories (WHO TRS 1052, Annex 4).

4.7. Validity of test results

The validity of results was ensured by the laboratory through a procedure that encompassed the review of various activities, including:

- Use of reference substances or reference materials
- Verification of measuring and testing equipment
- Implementation of appropriate quality control checks
- Performance of replicate tests or calibrations using the same or different methods
- Retesting of retained samples, when applicable.
- Review of all raw data and reported results.

If the analysis of monitoring data revealed results outside predefined criteria, appropriate actions were taken to prevent the reporting of incorrect results.

4.8. Out-of-specification results

Upon identifying a suspected OOS result, the supervisor, along with the analyst or technician, undertook a review of the procedures applied during the testing process using a checklist before initiating any retesting. This was conducted in accordance with SOP for Investigation of OOS and OOT, issued on 21 May 2025.

The investigation ensured that:

- If stable, the original sample preparations were not discarded until completion of the investigation.
- The applicable procedures were correctly applied and followed; an examination of the raw data was undertaken to identify any discrepancies.
- Calculations were verified.
- The equipment used was qualified and calibrated, and acceptable system suitability tests were performed.
- The appropriate reagents, solvents, and reference substances were used.
- The correct glassware was utilized.

The identification of an error that caused an aberrant result invalidated the result, and a retest of the sample, to be conducted by the same analyst or technician, was considered necessary.

Suspected OOS results were only rejected if they were clearly attributed to an identified error. In cases where the investigation remained inconclusive, a confirmatory determination was performed by another trained analyst. Obtaining a similar result indicated a confirmed OOS outcome. If available, hypothesis testing was considered to better define the root cause.

All investigations and their conclusions were recorded. In the event of an error, root cause analysis was performed, and any corrective actions were documented, implemented, and recognized as risks and opportunities for improvement.

4.9. Reporting of results

The study supervisor compiled the analytical test report, in hard copies, containing the analytical test results, for approval by the QA Head or designated person. Subsequently, the dossier containing all the information pertaining to the sample, including the origin, chain of custody, and analytical data, was archived.

Any amendments or changes to the original analytical test report required the issuance of a new document, where:

- Any change of information was identified and dated.
- The reason for the change was included in the new corrected document.
- The new report was uniquely identified and contained a reference to the original document it replaced.

The laboratory did not issue a separate test report. Instead, the samples' CoAs, including the Post-Importation CoA, served as the test reports. These CoAs included the following information: product name, date of manufacture, lot number, date of expiry, pack size, method number (as per the manufacturer's or laboratory's method), sample description, limits (specifications), and the test results. These were noted in the CoA for each type of testing, such as assay, identification, and degradation.

If any deviation was raised during testing, the deviation ID number was also recorded on the CoA. The status of the product—whether released or rejected—was indicated on the certificate. The product/CoA was authorized by the "Release Pharmacist," who had been contracted with the laboratory through the Oracle system. Following the release, the product was moved from quarantine to released status, allowing distribution to commence.

4.10. Nonconforming work

Refer to section 1.7.

4.11. Retained samples

The retained samples were stored in their original packaging, labelled as "Retained," and kept separately in order of expiry date. Samples were retained for one year after their expiry date.

The laboratory received samples from the local manufacturing site via the respective driver. Upon receipt, each sample was assigned a number by logging it in the sample receipt logbook and was then forwarded to the laboratory. The laboratory retained only those samples for which it was responsible for release, which were post-import products.

Sample disposal criteria were defined as one year after the expiry date.

5. Safety rules

Environmental health and safety policies were followed to protect staff, the public, and the environment.

General rules for safe working were defined in the relevant SOPs. Safety data sheets were made available to staff before testing. Protective clothing, including laboratory coats, eye protection, masks, and gloves, was available and suitable for use.

Firefighting and first aid training were conducted. Staff were familiar with firefighting equipment, including fire extinguishers.

Smoking, eating, and drinking in the laboratory were prohibited.

All chemical containers were appropriately labelled, with prominent hazard warnings where applicable (e.g., “poison,” “flammable,”). Adequate insulation and spark-proofing were ensured for all electrical wiring and equipment, including refrigerators.

Safety rules for handling compressed gas cylinders were observed.

Miscellaneous	
Assessment of the Laboratory Information File	The Laboratory Information File was submitted and reviewed.
Annexes attached	N/A

Part 3 – Conclusion – 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 ***Adcock Ingram Healthcare (Pty) Ltd – Research, Development & Implementation***, located at ***1 Sabax Road, Aeroton, Johannesburg, 2013; 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. 1. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-seventh Report, Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052), Annex 4.
   Short name: WHO GPPQCL Guidelines, TRS No 1052, Annex 4
   https://www.who.int/publications/i/item/9789240091030

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
   https://www.who.int/publications/m/item/trs961-annex2

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
   https://www.who.int/publications/m/item/annex-4-trs-929

4. 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/m/item/annex-4-trs-

5. 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***
   https://www.who.int/publications/m/item/trs986-

6. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report, Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2.
   Short name: WHO TRS No. 957, Annex 2
   https://www.who.int/publications/m/item/annex-2-trs-957

7. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report, Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3.
   Short name: WHO TRS No. 957, Annex 3
   https://www.who.int/publications/m/item/trs957-annex3

8. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report, Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 6.
   Short name: WHO TRS No. 961, Annex 6
   https://www.who.int/docs/default-source/medicines/norms-and-standards/guidelines/production/trs961-annex6-gmp-sterile-pharmaceutical-products.pdf

9. 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
   https://www.who.int/docs/default-source/medicines/norms-and-standards/guidelines/production/trs961-annex7-transfer-technology-pharmaceutical-manufacturing.pdf?sfvrsn=2e302838_0

10. Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report, Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 96, Annex 9)
    Short name: WHO TRS No. 961, Annex 9
    https://www.who.int/publications/m/item/trs961-annex9-modelguidanceforstoragetransport

11. 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
    https://www.who.int/publications/m/item/trs943-annex3

12. Guidelines on heating, ventilation, and air-conditioning systems for non-sterile 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
    Short name: WHO TRS No. 1010, Annex 8
    https://www.who.int/publications/m/item/Annex-8-trs-1010

13. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report, Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2.
    Short name: WHO TRS No. 981, Annex 2
    https://www.who.int/publications/m/item/trs981-annex2

14. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report, Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3.
Short name: WHO TRS No. 981, Annex 3
https://www.who.int/publications/m/item/annex-3-trs-981

15. WHO guidelines for preparing a laboratory information file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report, Geneva. WHO Technical Report Series, No. 961, 2011, Annex 13.
Short name: WHO TRS No. 961, Annex 13
https://www.who.int/docs/default-source/medicines/norms-and-standards/guidelines/quality-control/trs961-annex13-guidelines-preparing-laboratory-information-file.pdf?sfvrsn=54d1f397_2

16. WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report, Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4.
Short name: WHO TRS No. 992, Annex 4
https://www.who.int/publications/i/item/9789241209922

17. WHO Technical supplements to Model Guidance for storage and transport of time – and temperature–sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report, Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5.
Short name: WHO TRS No. 992, Annex 5
https://www.who.int/publications/m/item/trs992-annex5

18. 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
https://www.who.int/publications/m/item/trs1010-annex10

19. Good chromatography practices. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report, Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4.
Short name: WHO Good chromatography practices
https://www.who.int/publications/m/item/trs1025-annex4

20. Good manufacturing practices: guidelines on validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-third report, Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1019), Annex 3.
Short name: WHO TRS No. 1019, Annex 3
https://www.who.int/publications/m/item/trs1019-annex3

21. WHO model certificate of analysis. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second report, Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 4.
Short name: WHO TRS No. 1010, Annex 4
https://www.who.int/publications/m/item/trs1010-annex4

22. 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 No 1033, Annex 3
https://www.who.int/publications/m/item/annex-3-trs-1033

23. Guidelines on pre-approval inspections. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-sixth report, Geneva, World Health Organization, 2002 (WHO Technical Report Series, No. 902), Annex 7
Short name: WHO TRS No 902, Annex 7
https://www.who.int/publications/m/item/trs902-annex7

24. Prequalification of quality control laboratories: procedure for assessing the acceptability, in principle, of quality control laboratories for use by United Nations agencies. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-first report, Geneva, World Health Organization, 2017 (WHO Technical Report Series, No. 1003), Annex 3
Short name: WHO TRS No 1003, Annex 3
https://www.who.int/publications/m/item/annex-3-trs-1003