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Prequalification Team Inspection Services
WHO PUBLIC INSPECTION REPORT
Bio-Equivalence Study
WHOPIR

Part 1	**General information**
Organization details	
Company information	
Name and Address of Clinical Research Site	**Micro Labs Limited,** **Clinical Pharmacology Unit** Nos. 9 to 14, Katha Nos. 390/395, Situated at Kudlu Near Grama Panchayath Office, Singasandra Post Sarjapura Hobli, Anekal Taluk Bengaluru District, Bengaluru - 560068 Karnataka, India **Ecron Acunova Limited, located at** V Floor, MCODS Building, KMC Hospital, Attavar, Mangalore – 575 001, India, is related to the WHO application No. HA809. The site was inspected separately.
Name and Address of Bioanalytical Research Site	**Micro Labs Limited,** **Micro Advanced Research Centre** 2nd Floor, 58/3, Kudlu Village Anekal Taluk, Bangalore Karnataka - 560068 India
Name and address Statistical Site	**Micro Labs Limited** **Clinical Pharmacology Unit** Nos. 9 to 14, Katha Nos. 390/395 Situated at Kudlu Near Grama Panchayath Office Singasandra Post Sarjapura Hobli, Anekal Taluk Bengaluru District, Bengaluru - 560068 Karnataka, India
Corporate address of Organization	**Head Office:** 31, Race Course Road Bangalore -560001 Karnataka, India Tel no. +91 80-22370451-57 Email: info@microlabs.in

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WHO product numbers covered by the inspection/ Product names/ Study numbers/ Study titles	**WHO application no. HA793**	Bioequivalence Study of Dolutegravir Dispersible Tablets 10 mg
	WHO application no. HA809	Bioequivalence study of Abacavir, Dolutegravir, and Lamivudine tablets for oral suspension 60mg/5mg/30mg
Sponsor	Micro Labs Limited, India	
Inspection details		
Dates of inspection	16 – 18 February 2026	
Type of inspection	Routine	
Introduction		
Summary of the activities	The facilities are primarily focused on conducting clinical trials and analyzing samples collected during Bioavailability and Bioequivalence (BA/BE) studies to support marketing authorization applications in various markets, including the United States, Europe, and Australia, for in-house-developed products.	
General information about the company and site	Micro Labs Limited is a private organization established by the late Mr. G. C. Surana and is currently led by Dr. Dilip Surana and Mr. Anand Surana. Founded in 1973, Micro Labs Ltd. is a fully integrated pharmaceutical company operating across the entire pharmaceutical value chain, including research and development, active pharmaceutical ingredients, finished formulations, and marketing and distribution in India and overseas.	
History	The CRO has been inspected by the US FDA, MHRA, and CDSCO since 2017. The previous WHO inspections took place in April and December 2022.	
Brief report of inspection activities undertaken	The following scope and study-related activities were reviewed: The company's history, clinical study performance, informed consent process, ethics committee approvals and correspondence, test article accountability, dispensation and storage, processing and handling of biological (plasma) samples collected during the study, equipment calibration, employee training, computer controls, and a tour of the facility.	

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	Regarding the analytical operations, coverage was provided to confirm the practices, personnel qualifications, and procedures used during method validation and analytical testing. A review of the clinical study data, analytical method validation, and analytical study data was conducted, along with a comparison of the source data to the study reports.
Scope and limitations	
Out of scope	Not applicable

Abbreviations	ADR	adverse drug reaction
	AE	adverse event
	ALCOA	attributable, legible, contemporaneous, original and accurate
	BA	bioanalytical
	BE	bioequivalence
	BDL	below detection limit
	CAPA	corrective actions and preventive actions
	CC	calibration curve
	CPU	clinical pharmacology unit
	CRA	clinical research associate(e)
	CRF	(electronic) case report form
	CRO	contract research organization
	CTM	clinical trial manager
	CoA	certificate of analysis
	CSR	clinical study report
	DQ	design qualification
	ECG	electrocardiogram
	GAMP	good automated manufacturing practice
	GCP	good clinical practice
	GLP	good laboratory practice
	GMP	good manufacturing practice
	HPLC	high-performance liquid chromatograph
	LC-MS/MS	liquid chromatography–mass spectrometry
	IB	investigator's brochure
	ICF	informed consent form
	ICH	International Conference on Harmonization
	(I)EC	(Independent) Ethics Committee
	IMP	investigational medicinal product

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ISF	investigator study file
ISR	incurred sample reanalysis
IQ	installation qualification
LIMS	laboratory information management system
LLOQ	lowest limit of quantification
LOD	limit of detection
MS	mass spectrophotometer
MVR	monitoring visit report
NRA	national regulatory agency
OQ	operational qualification
PIS	patient information sheet
PQ	performance qualification
PQS	pharmaceutical quality system
QA	quality assurance
QC	quality control
QRM	quality risk management
SAE	serious adverse event
SAR	serious adverse reaction
SOP	standard operating procedure
SUSAR	suspected unexpected serious adverse reaction
ULOQ	upper limit of quantification
URS	user requirements specifications

PART 2	SUMMARY OF THE FINDINGS AND COMMENTS

General section

1. Organization and management

A presentation was provided outlining the organization's activities in detail, including recent changes since the last WHO inspection. Separate presentations were delivered for clinical and bioanalytical departments.

The CRO established an in-house pathology laboratory in 2025; however, this facility was not used for the studies within the scope of this inspection. The clinical unit has been expanded by an additional 50 beds, which was also not related to the scope of the present inspection.

Certificate of BA study center was issued on 6 September 2021 and was valid for five years.

The CRO maintained organizational charts separately for CL and BA departments, depicting key positions and the names of responsible persons. The organizational chart was dated, authorized, and kept up to date.

There was a job description for each employee, including their responsibilities. It was randomly verified that each job description was signed and dated by the respective staff member to whom it applied.

A list of signatures of the authorized personnel performing tasks during each study was available and verified. The Delegation of Job Task for Study, specific to the Study related to the WHO application no. HA793 was reviewed. The names of delegated personnel, dates of delegation, signatures of the Principal Investigator, designation codes for each responsibility, and both full and short signatures were documented. Evidence of protocol training was available in the Protocol Training Form.

As of the time of the inspection, the Micro Labs CPU had conducted BE studies only for Micro Labs. For the study related to the WHO application no. HA793, a Master Service Agreement was available between the Sponsor (Micro Labs Limited, Mumbai, and Micro Labs Limited – Micro Advanced Research Centre, Bengaluru) and Micro Labs Limited CPU, Bengaluru, and Micro Labs Limited BA Facility, Bengaluru, dated 22 January 2021 and valid for 10 years. As stipulated in the agreement, study-specific task allocation was to be issued. The document was available for the study related to the WHO application HA793, dated 1 December 2022, and signed by both the sponsor and the CRO on the same date. The document included assigned responsibilities such as monitoring and data management.

2. Computer systems

An inventory of all computerized systems on the network was available, with clear identification of those that were GXP-regulated. Any changes to the network were documented.

The LIMS software application was implemented and used for the studies within the scope of the inspection. The application was used for the preparation of the sample sequence for sample analysis in the chromatography software application, as well as for the calculation of study data and batch acceptance. Study data were transferred directly from the chromatography software application to LIMS. Test actions related to the system qualification were randomly selected and verified, including the transfer of

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analytical data to the software and the corresponding audit trail challenges. The system was fully implemented in August 2024 and therefore applied only to the study related to the WHO application no. HA809.

Procedures for Computer System Validation, effective 29 March 2024, were established and available.

The Clinical Department started using an automated device for the measurement of BMI. An installation certificate was available, including the calibration dated 9 January 2023, issued by the service provider. A QC certificate was also available.

Regular updates to key software programs were performed, as required. These activities were carried out in accordance with the applicable SOP.

The physical location of the servers was identified on the respective layout. The server room was visited and found to be well organized.

Daily, weekly, and monthly backups were performed on tape in accordance with SOP for Backup.

The observation related to the computerized systems was adequately addressed in the respective CAPA plan.

3. Quality management

The site maintained a total of 100 SOPs, structured across several functional areas. These include 25 operational SOPs, 23 related to equipment, and 24 general SOPs. In addition, 11 SOPs fall under the Quality Assurance Unit, 8 under Data Management, 3 under Engineering, and 6 under IT.

QA personnel were not directly involved in trial-related activities. The QA unit for BA was separate from the QA unit for the clinical department, with distinct Heads and defined responsibilities. Quality Assurance activities at the site encompassed several key functions to ensure compliance and data reliability. These included maintenance and implementation of the Quality Manual, oversight of document control systems, and ensuring adherence to data integrity principles. QA was responsible for conducting internal audits to verify compliance with applicable procedures and regulatory requirements, as well as coordinating and supporting external audits and inspections. In addition, QA oversaw training activities to ensure that personnel were appropriately qualified and trained for their assigned responsibilities.

Both in-process and retrospective QA verifications (e.g., in bioanalysis, during preparation and testing of samples and standards) were performed in accordance with SOP for Internal Audits.

The observation related to the QMS was adequately addressed in the respective CAPA plan.

4. Archive facilities

The CRO maintained a secure storage facility for archiving trial-related documents, equipped with temperature and humidity control and pest control measures. Overall, the CRO ensured the safety and integrity of the documentation through comprehensive security measures.

The SOP for Archival, Retrieval, Re-archival, and Retention of Documents, applicable to the CPU archive, covered both paper and electronic records, including study-related documents, facility-related documents, and SOPs. Document retention periods were defined in accordance with regulatory requirements, with a minimum of 10 years (USFDA), 15 years (WHO, EU, MHRA, ANVISA, TGA), and up to 25 years for Canada. Archival submission and retrieval records were reviewed during the inspection.

Pest control activities were performed twice monthly by a service provider under an agreement dated 19 December 2024 and valid for two years. Service reports for the previous three months were reviewed and included spray treatment, gelling, baiting, and monitoring for common pests.

Environmental conditions in the archive room were monitored twice daily using a thermohygrometer and were recorded in the temperature and humidity logbook. Acceptance criteria were defined in the respective SOP. Records reviewed for the previous three months were within the specified limits.

5. Premises

During the inspection, a tour of the facility was conducted.

The facilities were maintained in a clean condition and had adequate lighting, ventilation, and environmental control. Floors, walls, and working bench surfaces were designed to allow easy cleaning and decontamination.

Clinical trials were conducted under conditions that ensured adequate safety for the subjects. The selected site was appropriate to the potential risks involved.

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The CRO had sufficient space to accommodate the personnel and activities required for the conduct of the studies. The trial site had adequate facilities, including laboratories and equipment. Entry to the facility was restricted and controlled through keycards. Emergency evacuation procedures were in place and ensured.

Areas where clinical activities were conducted included a pharmacy in which investigational products were stored under appropriate conditions. Access to the pharmacy was restricted through controlled entry and exit. Appropriate records of each entry and exit were maintained.

Temperature and relative humidity in the pharmacy humidity chamber were monitored using the digital monitoring system. The system recorded data at 30-minute intervals and was reviewed daily by the pharmacist through printed records. The identification of the reviewer and approver was recorded in the system. Records for the previous three months were reviewed during the inspection.

The established limits were 21–25°C for temperature and 55–65% for relative humidity. Isolated RH excursions were noted; however, these were not continuous and generally occurred at single intervals only.

Laboratory premises were designed to suit the operations to be carried out in them. Sufficient space was provided to avoid mix-ups, contamination, and cross-contamination. Adequate storage space was available for samples, standards, solvents, reagents, and records.

6. Personnel

A sufficient and qualified team of medical, paramedical, technical, and clerical staff was available to support the trial and to respond effectively to foreseeable emergencies. At all stages of the trials, including night shifts, qualified and trained personnel were available to ensure that the rights, safety, and well-being of subjects were safeguarded and that appropriate care was provided in emergencies. For specific activities, contract workers were employed to complement the team's capabilities.

Randomly selected current curricula vitae and training records of personnel involved in trial-related activities, including both full-time and contract workers, were reviewed and verified during the inspection.

7. Clinical phase

The clinical and bioanalytical sites were located within walking distance on the same premises.

The CPU was equipped with 62 beds and a two-bed ICU serving the entire unit. The facility included four housing areas: Housing I (24 beds), Housing II (14 beds), Housing III (24 beds), and Housing IV (50 beds), the latter pending CDSCO approval and not in use at the time of the inspection. Beds were equipped with corded handsets, and washrooms and bathrooms were fitted with emergency pull-cord modules to allow subjects to alert CRO staff when required. The housing areas were access-controlled and equipped with bedside and toilet alarm systems, outward-opening toilet doors, and emergency exits. Nurse stations were located on the Ground and First floors to monitor the entry and exit of study participants. Emergency trolley medicines were checked monthly, and environmental conditions were monitored.

Facilities for changing and storing clothes and for washing and toilet purposes were well-ordered, easily accessible, and appropriate for the number of users. Toilets were lockable and alarmed, and the doors were designed to allow opening from the outside in the event of a medical emergency.

The sample processing room located on the ground floor was visited during the inspection. The room was equipped with two centrifuges and two −65°C deep freezers, all with valid calibration status. Temperature monitoring of the deep freezers was performed using the digital monitoring system. Hotspot locations identified during temperature mapping were marked and verified. An alarm challenge performed during the inspection triggered an audible alarm and notification to responsible personnel. Evidence of the alarm notification was reviewed.

Access to the randomization list was restricted to the pharmacist in charge of the study, the QA unit, and the study investigator. The list was maintained in the pharmacy as a hard copy, and its distribution was documented.

During the Study related to the WHO application HA793, three standby hospitals were identified for emergency management, and agreements with all three were available.

The equipment used was appropriately calibrated at predefined intervals. It was randomly verified that the defibrillator and oxygen meter were calibrated annually, and oxygen cylinder pressure was checked prior to subject check-in and on a monthly basis.

8. Clinical laboratory

During the conduct of the Dolutegravir study, all pathological samples were analyzed by the external clinical laboratory.

The internal clinical laboratory was established at the end of 2024 and obtained NABL certification in December 2025.

Accreditation certificates for the external laboratory were reviewed. NABL accreditation (ISO 15189:2012 for Medical Testing) was valid from 3 February 2022 to 2 February 2024 and subsequently from 3 February 2024 to 31 December 2025. CAP certificates were available, with one expired on 2 May 2024 and another valid until 2 May 2026.

An on-site vendor re-qualification audit of the external laboratory was conducted by the CPU QA team on 1 August 2023, following a virtual audit in 2022. The audit documentation was reviewed. The audit covered facility, equipment, documentation, sample management, quality systems, personnel training, certifications, and data handling. No observations were raised.

Laboratory reports were received via a digital platform, with access provided to the Clinical department for review and printing. Following termination of the contract, access to the system was discontinued.

9. Ethics

Trials were approved by the independent ethics committee on 22 November 2023, before initiation of the study related to the WHO application no. HA793. The independence of the IEC from the sponsor, investigator, and CRO was verified through the respective member list.

Detailed minutes of the meetings documented the discussions, recommendations, and decisions of the IEC. The IEC was provided with sufficient time to review the protocols, informed consent forms, and related documentation.

<u>Informed consent form</u>

Information for study participants was provided in English, Hindi, and Kannada, both orally and in writing, at a level appropriate to their understanding.

Informed consent was obtained in writing from each subject prior to initiation of any trial-related activities. The information clearly stated that participation was voluntary and that subjects could withdraw at any time without providing a reason. Reasons for withdrawal were documented in the study records.

Information on insurance coverage and procedures for compensation or treatment in the event of trial-related injury or disability was available in the insurance policy. Subjects were allowed to discuss potential side effects or reactions with a physician prior to participation.

Certificates of translation of the ICF were reviewed. A certificate for translation of the English ICF into Hindi, Kannada, Tamil, and Telugu was available. Translation was performed by Translation Services.

The observation related to ICF was adequately addressed in the respective CAPA plan.

10.Monitoring

The study was monitored by an external monitor appointed by the sponsor. The monitor was appropriately qualified to ensure that the study was conducted in accordance with the protocol, GCP, GLP, and applicable ethical and regulatory requirements, including verification of CRF completion and accuracy of recorded data.

Monitoring visits were conducted on check-in and dosing days for Period I and Period II of the respective study, as confirmed by the Entry and Exit Logbook. An Audit/Monitoring Log was available. Monitoring reports for both periods were reviewed, with no observations raised. A monitoring certificate was also available.

11.Investigators

The principal investigator was responsible for the clinical conduct of the study, including clinical aspects of the study design, administration of the investigational products, communication with local authorities and the ethics committee, and signing of the protocol and final study report.

12.Receiving, storage, and handling of investigational drug products

Receipt of the investigational medicinal product was documented using the “Receiving of IMP” form. The form recorded the project number, type of IMP, date and time of receipt, data logger ID, accompanying documents (e.g., Certificate of Analysis, cover letter, T license, and GMP certificate where applicable, and purchase invoice if available), quantity received, and signatures with dates of the pharmacist and PI.

Pharmaceutical products were stored under conditions specified in the official product information provided by the sponsor. Storage conditions were monitored using the ICDAS system in the humidity chamber.

The IPs were appropriately labelled, with labels affixed to the containers to ensure that information remained available after removal of the lid.

Adequate procedures for labelling and documenting IP administration were established. Labels with a tear-off portion were used to verify that each subject received the dispensed product. One portion of the label was affixed to the container, and the corresponding portion was attached to the CRF at the time of dosing.

Empty containers were labelled separately for test and reference products and were stored in a segregated and secure area within the humidity chamber to prevent any potential mix-ups until dispensing.

Dispensing and packaging procedures were performed in accordance with established requirements. Dosing was conducted in compliance with SOP for Dosing of IMP.

The surface used for handling the product was cleaned prior to dispensing. All product containers (full or empty), individual dosage units, labelling materials, and any unrelated materials were removed from the area. A second person verified that the area was clean and clear before containers were introduced and opened. IMPs were handled using appropriate utensils. Tablets were dispensed into containers in accordance with the randomization list for the test or reference product, as applicable. The test and reference products were handled at separate times, including the respective labelled containers. All steps were documented sequentially in detail. The dispensing area and its surroundings were cleaned immediately before and after dispensing each product, including within the same study.

Investigational product accountability and dispensing records were maintained. Each activity was documented at the time of performance, including records of doses administered, returned, or destroyed, and verification of each step by a second person.

Investigational product reconciliation after dosing was verified by a second responsible person. Samples of the product in the original container were retained for possible confirmatory testing for at least one year after the expiry date of the newest product. Sample retention was defined in SOP Handling of IMP and specified in the contract between the sponsor and the CRO. Dispensed products that were not administered were also retained.

13. Case report forms

Randomly selected CRFs from the study were reviewed. The data collected for each volunteer were specified in the trial protocol.

During the review, inclusion and exclusion criteria were verified, including BMI records, laboratory reports, ECGs, and X-ray results. Alcohol and urine drug screening results were documented. Dosing of test and reference products was verified against the randomization schedule, including verification of tear-off labels and the PI's signature.

Adverse events were documented in the CRF, including treatment provided, assessment, and resolution.

14. Volunteers, recruitment methods

Volunteers were required to register in the Entry and Exit Logbook at the security post. Cross-participation was verified using software with fingerprint and photograph identification. Informed consent was obtained prior to registration. Volunteer identity was further verified through the in-house database.

A physical examination room was available. Two ECG units were in use and calibrated annually, with controlled user access.

15. Food and fluids

Meals provided to study subjects were standardized, controlled, and scheduled in accordance with the clinical trial protocol. Standardized meals, snacks, and drinks were arranged through a contracted catering service. Timing and quantity of food and fluid intake were recorded, and subjects were questioned regarding consumption prior to sample collection.

A dietician was responsible for weighing meals prior to serving, and the weighing balance was calibrated annually. During the study related to the WHO application no. HA793, catering services were provided under an agreement dated 4 July 2020 and renewed on 26 August 2021 for five years.

The qualification of the dietician was verified through the relevant training records, CV, and job description on file.

16.Safety, adverse events, adverse event reporting

The records of use of concomitant medication for the study related to the WHO application no. HA793 was available and reviewed.

No serious adverse events were reported. A total of eight adverse events were recorded involving seven subjects, and no subjects were withdrawn due to adverse events.

First-aid equipment and appropriate rescue medication were available in the ICU and ready for emergency use at the study site. Any treatment given to a subject was documented and included in the CRF and the supporting documentation in the ICU.

The CRO had adverse event registration and reporting forms as part of the CRF.

Bioanalytical section

The inspection focused on the study related to the WHO application no. HA809, including the associated validation projects. Spot checks were also conducted for the study related to the WHO application no. HA793. In particular, the following records and activities were randomly reviewed:

- Source documentation and raw data for validation of the bioanalytical methods.
- Analysis of subject plasma samples as well as the respective electronic data.
- Audit trails for electronic data capture and handling related to the BE studies.
- Results of calibration standards, quality control samples, and subject plasma samples in analytical runs, along with the chromatograms generated from the analytical runs.
- Preparation of analyte stock solutions, calibration standards, QCs, and internal standards.

Furthermore, chromatograms and their integrations, the absence of signals in blank samples, and the absence of unexplained interruptions in the injected sequences were verified. The reason for the study sample repeat analyses and the instrument failures was reviewed. The provisions and the documentation of the ISRs were confirmed. The documentation and justification for the reinjection of the analytical runs were verified and compared to the provisions.

During the review of the study documentation, the inspection team received adequate support from knowledgeable and transparent personnel, mainly the Head of the Bioanalytical Laboratory.

17.Method development, Method validation & Analysis of study samples

An analytical plan was available as the basis for method validation. Stable isotope-labelled internal standards were used in the MS methods, and an anticoagulant was applied during sample collection.

Study related to the WHO application no. HA809

The determination of abacavir and lamivudine in human plasma in the presence of dolutegravir was conducted in accordance with the approved bioanalytical study plan. The analytical method was validated as per the corresponding method validation protocol, and the results were documented in the respective method validation reports and addendum.

Similarly, the determination of dolutegravir in human plasma in the presence of abacavir and lamivudine was performed in accordance with the approved bioanalytical study plan. Method validation was carried out as per the applicable validation protocols, and details were documented in the corresponding validation reports and addenda.

Validated Excel sheets were used to calculate batch acceptance for this study.

Study related to the WHO application no. HA793

The validated method for the determination of dolutegravir in human plasma was applied in accordance with the approved bioanalytical study plan. Method validation was performed as per the corresponding validation protocol, and the results were documented in the associated method validation report and addendum.

During method validation in accordance with the applicable SOP, an extended batch run, comparable in length to routine analytical runs, was performed. The extended batch for Lamivudine and Abacavir was verified.

Sample processing was documented in the respective forms. A note to file was prepared, when applicable, to document any unexpected activity during sample processing.

Data supporting the stability of samples under the stated storage conditions and period were available prior to study initiation, with the exception of long-term stability, which was completed before issuance of the study reports.

The method validation was reviewed and included assessment of precision and accuracy, sensitivity, selectivity, matrix effect, calibration curve performance, autosampler carry-over, dilution integrity, freeze–thaw stability, bench-top stability, autosampler stability, wet extract stability, dry extract stability, evaporator stability, whole blood stability

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(including collection, storage, retrieval, centrifugation, QC preparation, and sample processing), haemolytic and lipemic effect, recovery, and reinjection reproducibility. Partial validation was performed as required.

The matrix used for method validation was the same as that of the study samples, including anticoagulants and additives. Plasma for the study related to the WHO application HA809 was provided in-house, whereas plasma for the study related to the WHO application HA793 was purchased from an external supplier. Documentation related to procurement and handling of plasma, including invoice/collection, transport, storage, retrieval, pooled matrix preparation, and consumption, was reviewed. The supplier had undergone an on-site audit in 2019 and a remote audit in 2022. At the time of inspection, only in-house plasma was provided to be used during the analytical methods.

Documentation for preparation of stock solutions, spiking solutions, and working solutions for CC, QC, and IS was available and was randomly verified for Lamivudine and Abacavir. Consumption of CC and QC sets, including both used and unused solutions, was recorded in the LIMS. Storage and retrieval were documented in the respective Deep Freezers' logbooks. Consumption of reference standards was recorded in the corresponding logbook. The logbook entries for Dolutegravir and Dolutegravir D3 were randomly verified for the study related to the WHO application HA809.

Each analytical run included calibration curve standards, QC samples distributed throughout the run, and subject samples, which were processed simultaneously. The processing sequence was predefined and documented. For the study related to the WHO application HA809, the sequence was generated in LIMS and transferred to an analyst for analysis. All samples from a given subject across all trial periods were analysed within the same run.

Acceptance of analytical runs was based on review of analyte retention times, accuracy of calibration standards and QC samples, peak integration, and IS peak areas, in accordance with the applicable SOPs.

A system suitability and stabilization test was performed prior to the start of daily runs in accordance with the applicable SOP.

Any reintegration was documented using the Reintegration Record Form, issued by QA. One reintegration was identified for Lamivudine (subject 9), which was appropriately documented. The reintegration was performed to correct the integration of CS1 and was applied consistently throughout the run.

The reconciliation form for the study related to the WHO application HA809 was reviewed and compared with the corresponding logbook for issuance of templates used in study activities. The process was performed under QA supervision.

Incurred Sample Reanalysis was performed during and/or after completion of subject sample analysis and was not conducted on the same day as the initial analysis of the respective samples. At least 10% of samples were selected for ISR for the first 1000 samples and 5% for the remaining samples. A designated person identified and reviewed samples for ISR. At least two samples per period from all accepted analytical batches were selected as incurred samples: one sample near Cmax and one from the elimination or terminal phase with a concentration above the LQC. Acceptance criteria were defined in SOP for Incurred Sample Reanalysis.

System audit trail review was performed retrospectively by QA within the scope of the inspection. Training was provided to the responsible personnel in accordance with the applicable SOPs.

It was verified during the inspection that, in cases where a subject was withdrawn due to an adverse event after receiving at least one dose of the study medication, the subject's plasma/serum concentration data were provided.

It was further verified that specific procedures were in place for subjects with pre-dose concentrations greater than 5% of the corresponding Cmax. Subjects with pre-dose concentrations equal to or less than 5% of Cmax were included in the statistical analysis without correction, in accordance with the defined procedures.

18.Sample collection, storage, and handling of biological material

The specification of samples (blood plasma), including sampling method, volume, and number of samples, was defined in the clinical trial protocol and in the information provided to the volunteers. SOP for Receipt, Handling, Storage, and Disposal of Study Samples defined the corresponding procedures in the BA laboratory.

Blood sampling was conducted in the presence of QA, QC, and CRA personnel to ensure procedural compliance and oversight. Both planned and actual sampling times were recorded directly in the paper CRFs, using synchronized clocks available in the housing area to ensure consistency and accuracy of time documentation.

Vacutainers were pre-labelled by the clinical department prior to sample collection and verified by QC personnel before use. Labelling ensured the correct identification and

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traceability of collected PK samples. During sample processing, samples were aliquoted into cryovials and labelled prior to transfer to the bioanalytical laboratory. The labels, generated by the BA team through the LIMS system and shared with the clinical department, included unique barcodes used for sample receipt, tracking, and documentation within the system, ensuring traceability throughout the bioanalytical process, in accordance with the respective SOP.

All storage conditions, including freezer temperatures, were controlled, monitored, and recorded throughout storage and transportation. Records for storage, retrieval, and restorage of samples were maintained. Samples were prepared in duplicate aliquots, shipped, and stored separately. For the ALD study, samples were divided into three aliquots: Aliquot I for abacavir and lamivudine analysis, Aliquot II for dolutegravir analysis, and Aliquot III as backup for dolutegravir. Aliquot III was shipped separately on 26 November 2024 for ISR (run 7) analysis. Evidence of sample transfer from Ecron to Micro Labs, including shipment conditions and verification records, was reviewed. Receipt, retrieval, and restorage of samples used for ISR 7 were verified in Deep Freezer 01, designated for storage of Aliquot III.

It was noted during the inspection that the LIMS system allows recording of up to two aliquots; use of more than two aliquots requires manual naming within the system.

The remaining PK aliquots were stored in the cold walk-in chamber within the clinical department.

The observation related to sample collection was adequately addressed in the respective CAPA plan.

19.Data processing and documentation

Integration settings were science-based and justified. The smoothing factor was set at a level that did not mask potential interferences or alter peak geometry.

Criteria for acceptance and exclusion of CC standards and QC samples, as well as batch acceptance, were defined in the applicable SOP. Source data for all analytical runs included documentation of the initial evaluation of runs, including calibration samples, where reanalysis was performed. The calibration range was appropriately truncated.

Internal standard variations were trended and considered in the verification of result validity. LIMS was used for batch acceptance calculations, including ISV assessment, sample sequence generation, and aliquot labelling.

Full audit trails were always activated on all analytical instruments before, during, and after the method validation and the studies of interest. Audit trail review of the chromatography systems took place in accordance with an established checklist.

All original analytical raw data (e.g., calculations, chromatograms, and their associated audit trails) were documented in LIMS that ensured traceability concerning the sample number, equipment used, date and time of analysis, and the name(s) of the technician(s). All audit trail files were retained (e.g., results table audit trail, project audit trail, and instrument audit trail).

Each data point was traceable to a specific sample, including sample number, time of collection of the sample, time of centrifugation, time when the sample was placed in the freezer, and time of sample analysis, to be able to determine whether any aberrant results might have been caused by sample mishandling.

20.Good laboratory practices

A tour of the facility was performed to verify the security configuration of the Chromatography software systems and the respective instruments.

Pharmacokinetic, statistical calculations and reporting section

21.Pharmacokinetic, statistical calculations

A presentation was provided outlining the process and procedures for randomization, as well as statistical and PK analysis.

The processes for randomization, PK evaluation, and statistical analysis were defined and controlled.

Randomization was initiated by the pharmacist through a formal requisition form and approved by the PI. The approved request was submitted to the biostatistician, who generated the randomization code in accordance with the predefined SOP and executed the program in the presence of QA. The randomization schedule was reviewed, QA-verified, and retained under controlled access in the pharmacy.

Following QC/QA review, bioanalytical concentration data were transferred to the biostatistician in read-only format. Actual sampling times were incorporated, and the dataset was organized in accordance with the relevant SOP. Data were processed using SAS, reviewed by the biostatistician, and verified by QA against the randomization schedule and sampling records prior to further analysis.

PK analysis was performed using WinNonlin to generate concentration–time profiles and calculate pharmacokinetic parameters as specified in the protocol. Statistical analysis was conducted in SAS under secure access, with controlled file management, output review, and documented final approval.

Transfer of timepoint information was performed using a paper-based form prepared by the CRA. The form documented the planned and actual sampling timepoints and was formally handed over to the statistician for data processing.

The observation related to statistical analysis procedures was adequately addressed in the respective CAPA plan.

22.Study report

No discrepancies were identified between the randomly reviewed results presented in the report and the original (raw) data.

The study report included the bioanalytical section of the trial, comprising a description of the analytical method and its validation.

The PI approved the clinical study report prior to the transfer of data to the statistical department.

Bioanalytical reports were approved by the responsible staff and management.

Monitoring and audit reports were available prior to the issuance of the final study report.

Miscellaneous	
Samples taken	***Not applicable***
Assessment of the CRO master file	The Site Master File for the Clinical Pharmacology Unit & the Site Master File for the Bioanalytical Laboratory were available.
Annexes attached	***Not applicable***

Part 3	Inspection outcome

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report of Micro Labs Limited, located at the following addresses, was considered to be operating at an acceptable level of compliance with WHO GCP/GLP/BE guidelines.

Clinical Pharmacology Unit
Nos. 9 to 14, Katha Nos. 390/395, Situated at Kudlu
Near Grama Panchayath Office, Singasandra Post
Sarjapura Hobli, Anekal Taluk
Bengaluru District, Bengaluru - 560068
Karnataka, India

Micro Labs Limited,
Micro Advanced Research Centre
2nd Floor, 58/3, Kudlu Village
Anekal Taluk, Bangalore
Karnataka - 560068
India

The deficiencies observed during the inspection, as listed in the full report, were addressed by the CRO to a satisfactory level before 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 guidelines referenced in the inspection report

1. Guidance for organizations performing in vivo bioequivalence studies. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 9.
   Short name: WHO BE guidance or ***TRS996 Annex 9***

2. Good clinical laboratory practice (GCLP), WHO on behalf of the Special Programme for Research and Training in Tropical Diseases. Geneva, 2009
   Short name: WHO GCLP

3. Guidelines for good clinical practice for trials on pharmaceutical products. WHO Technical Report Series, No. 850, 1995 (pp. 97–137).
   Short name: WHO GCP

4. Handbook – Good Laboratory Practice (GLP): quality practices for regulated non-clinical research and development – Annex I: The OECD Principles on GLP, 2nd ed., 2009. ***Short name: OECD GLP***

5. Standards and operational guidance for ethics review of health-related research with human participants. Guidance Document. Geneva, World Health Organization, 2011.
   Short name: WHO Ethics Committee Guidance

6. Guidelines for the preparation of a contract research organization master file, WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 7.
   Short name: WHO CROMF Guidelines or ***TRS No. 957, Annex 7***

7. 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. 961), Annex 9.
   Short name: WHO storage and transport guidance or ***TRS 961 Annex 9***

8. Glove use information leaflet, Patient Safety, Save lives clean your hands. Geneva, World Health Organization, 2009 (revised).
   Short name: Glove use information leaflet

9. Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability. Republication of multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability. WHO Technical Report Series No. 992, Annex 7 with a new appendix 2. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-first Report Geneva, World Health Organization, 2017 (WHO Technical Report Series, No. 1003), Annex 6.
   Short name: TRS 1003 Annex 6

10. Good chromatography practice. 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 TRS No. 1025, Annex 4

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

12. Declaration of Helsinki, World Medical Association Declaration of Helsinki, Ethical principles for medical research involving human subjects, Bulletin of the World Health Organization, 2001 (79(4)).
Short name: Declaration of Helsinki

13. Bioanalytical Method Validation and Study Sample Analysis M10, ICH Harmonised Guideline, Final version, Adopted on 24 May 2022
Short name: ICH M10

14. Guideline for Good Clinical Practice, E6 (R3), ICH Harmonised Guideline, Adopted 6 January 2025
Short name: ICH GCP E6 (R3)

15. Good Manufacturing Practices: Guidelines on validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3.
Short name: WHO TRS No. 1019, Annex 3

16. Supplementary guidelines on good manufacturing practices: validation, WHO Expert Committee on Specifications for Pharmaceutical Preparations, Fortieth report, World Health Organization, 2006 (Technical Report Series, No. 937), Annex 4.
Short name: WHO No. 937, Annex 4