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

Part 1	**General information**
Organization details	
Company information	
Name and Address of Clinical Research Site	Vimta Labs Ltd 142, IDA, Phase II Cherlapally, Hyderabad 500051 Telangana, India
Name and Address of Bioanalytical Research Site	Vimta Labs Ltd 142, IDA, Phase II Cherlapally, Hyderabad 500051 Telangana, India
Name and address Statistical Site	Vimta Labs Ltd 142, IDA, Phase II Cherlapally, Hyderabad 500051 Telangana, India
Corporate address of Organization	142, IDA, Phase II Cherlapally Hyderabad, India -500051 Phone: +91-40-2726-4141, Fax: +91-40-2726-3657, Email: vimtahq@vimta.com
GPS coordinates	Latitude: 17.470930 Longitude: 78.602480
WHO product numbers covered by the inspection/ Product names/ Study numbers/ Study titles	**WHO application no. NT022** Bioequivalence Study of Praziquantel tablets 600 mg **WHO application no. HA680** Bioequivalence Study comparing Dolutegravir Tablets 50 mg
Inspection details	
Dates of inspection	9-12 September 2025

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Type of inspection	Routine
Introduction	
Summary of the activities	At Vimta Labs Limited, Cherlapally, Bioavailability and Bioequivalence (BA/BE) studies are conducted in healthy volunteers. These studies cover a wide range of therapeutic categories, including but not limited to antihypertensives, antiepileptics, anti-inflammatories, antifungals, local anesthetics, oral and nasal inhalations, lipid-lowering agents, proton pump inhibitors, antiretrovirals, and anthelmintics.
General information about the company and site	Vimta Labs Ltd. was established in 1984 as a partnership firm and was converted into a limited company in 1991. Since then, both national and international companies have been supported through third-party testing, research, and outsourcing services. With the launch of the Clinical Research division in September 1994, continuous expansion was carried out in line with the growing pharmaceutical, food, and manufacturing sectors, while the presence in global markets was strengthened.
History	The CRO was inspected by the US FDA, CDSCO, and NPRA (Malaysia). A list of inspections was provided in Annex IV of the CRO MF. The last WHO inspection was conducted on 23 June 2008.
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. Regarding the Analytical operations, coverage was provided to verify practices, qualifications of personnel, and procedures utilized during the method validations 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	N/A

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Abbreviations	ADR	adverse drug reaction
	AE	adverse event
	ALCOA+	attributable, legible, contemporaneous, original and accurate, complete, consistent, enduring, available
	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–tandem mass spectrometry
	IB	investigator's brochure
	ICF	informed consent form
	ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
	(I)EC	(Independent) Ethics Committee
	IMP	investigational medicinal product
	ISF	investigator study file
	ISR	incurred sample reanalysis
	IQ	installation qualification
	LIMS	Laboratory Information Management System
	LLOQ	lowest limit of quantification

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	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 in which the activities of the organization were explained in detail.

The CRO had an organizational chart depicting key positions and the names of responsible persons. The organizational chart dated 30 August 2025 was authorized and kept up to date.

The CRO's license issued by CDSCO had expired, and a new application for approval was submitted within the due time and was under process.

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

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A list of signatures of the authorized personnel performing tasks during each study was available and verified. The CVs, training records, and confidentiality agreements of the staff were randomly verified during the inspection.

The principles of Good Laboratory Practices have sufficiently established the responsibilities of the test facility management. The CRO management was aware that, as the investigator was an employee of the CRO, some of the responsibilities usually assigned to the investigator similarly resided with the CRO management. It was ensured by the management that appropriate and technically valid SOPs were implemented and followed. The maintenance of a historical file of all SOPs was adequately organized.

The service agreement between the CRO and the sponsor was randomly reviewed, including the retention provisions for bio samples and study documentation.

2. Computer systems

A list of computerized systems used in the studies was provided; however, it was not prepared in the format specified in Appendix II of the respective SOP. During the inspection, a new list containing the required information was submitted. The CRO maintained this list as a controlled document, which included systems subject to revalidation, such as server- and web-based systems. It was appended to the applicable SOP and contained details of the last CSV, revalidation schedule, execution date, next due date, and the personnel responsible for performing and verifying the activities.

Procedures for Computer System Validation were established under SOP titled Computerized System Validation (CSV) to ensure that computerized systems were suitable for their intended purpose and were validated, operated, and maintained in accordance with the principles of GCP and GLP, as appropriate. The SOP described the life cycle of computerized systems, including pre-purchase planning (development of the URS and comparison with vendor specifications, vendor qualification, and risk assessment), post-purchase phase (IQ, OQ, and PQ), routine operation phase (change control, re-evaluation, calibration, maintenance, periodic review), and decommissioning.

A sufficient number of computers were available to enable personnel to perform data entry, data handling, required calculations, and compilation of reports. The computers had adequate capacity and memory for the intended use.

Access to the software systems containing trial-related information was controlled. The method of access control was specified, and a list of personnel with access to the database was maintained. Secure, unique, and individual-specific identifiers and passwords were used. For Analyst software, the Analyst Administrator Console was used for user and

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group management, access control, password policies, audit trail settings, and system configuration to ensure secure and compliant operation of the Analyst software.

The software programs used for key steps were suitable and validated for the intended use. Qualification and validation certificates were available under the user's supervision to confirm that the software had been validated for its intended use and developed in a controlled manner in accordance with the QA system. The qualification of the randomly selected systems was reviewed.

The specific user requirements, regulatory requirements for BE studies, the operating environment, and the system usage in studies were considered in the performance qualification. All life cycle phases were addressed. SOPs for the use of each software program in BE study activities were available. Access rights granted to investigator site staff were ensured to be in accordance with delegations and respective tasks.

Regular updates to key software programs were performed as required, following risk assessments on the potential impact on current data and qualification/validation status, in accordance with the applicable SOP.

Firewall settings, antivirus authentication requirements, and system monitoring were considered in accordance with the SOP for encryption of PCs and laptops.

Data backup was defined as the copying or archiving of files and folders to enable restoration in case of data loss. Detailed procedures for backup and storage were described in SOP for Server Data Back-up and Restoration Procedure – for Networked Software Systems, and SOP 84/77 for Data Back-up, Archival, Restoration, and Verification Procedure for Standalone Instruments. LabSolutions chromatography systems were the only standalone systems present on two units. The LabSolutions software system was used during the method validation of the Praziquantel study.

A detailed flowchart illustrating the network architecture, including the client/server structure and all relevant interfaces, was available. The network architecture flowchart included an overview of the layout with LANs and WANs, the client/server structure with connections and data flow highlighting server roles and functions, key interfaces such as LIMS and other critical systems, and security elements including firewalls and access control points. A separate data flowchart showing the main communication paths and system exchanges was also prepared.

The reliability and completeness of backups were verified through the restoration process. Periodic data verification was confirmed.

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3. Quality management

The CRO had established QA and QC systems with written SOPs to ensure that trials were conducted and data were generated, documented, and reported in compliance with the protocol, GCP, GLP, and applicable regulatory requirements. The CRO has been using electronic document management software for SOP management since 2024 and an electronic quality management system for managing QMS parameters such as change controls, deviations, and CAPA since 2019. SOPs were uploaded in a shared e-portal upon the inspectors' request.

The Quality Manual had been replaced by the CRO Master File with respective information about the QMS. QA personnel were not directly involved in trial activities. In-process QA audits did not replace the oversight that was required to be performed by other responsible personnel.

The QA unit was responsible for verifying study activities; ensuring quality systems were followed, reviewed, and updated; confirming availability and compliance with protocols and SOPs; checking data reliability and traceability; conducting and following up on self-inspections; ensuring contract facilities adhered to GCP/GLP; verifying the accuracy of trial reports; and promptly reporting audit findings. Both in-process and retrospective QA verifications, including bioanalysis, were performed in accordance with the respective SOP.

The audit trail queries or reports to be used for different systems and purposes were defined in the applicable SOP. The SOP specified which data required review, how data and modifications were presented in the audit trail, and which changes were acceptable in routine use. The audit trail review and its outcome were documented in the QA Checklist for Audit Trail Verification.

SOP for Management of Logbooks, Lab Note Books, Forms, Formats and Raw Data Sheets, effective 14 October 2023, was available and reviewed. The SOP described the controlled issuance of numbered logbooks, lab notebooks (LnBs), raw data worksheets, test data sheets, forms, and formats by QA to all VIMTA LABS' divisions/branch labs/facilities except the GLP Test Facility. It also included reconciliation of controlled documents and procedures for the use of uncontrolled and/or unnumbered forms and formats.

The quality management system included root cause analysis, trend tracking in bioanalysis, assurance of data integrity, and implementation of corrective and preventive actions (CAPA).

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

4. Archive facilities

The CRO maintained a secure interim storage facility for archiving trial-related documents, in addition to an off-site archiving facility, both under QA supervision. The in-house facility was equipped with fireproofing, humidity control, and pest control. Overall, the CRO ensured document safety and integrity through security measures. Furthermore, Vimta maintained the off-site archive facility 35 km from the site, which had been audited by the designated QA team. The report of the audit performed on 1–2 September 2025 was available and reviewed.

Archiving activities were managed in accordance with SOP for Archival Procedures. Access to archive storage areas was key-controlled and restricted to authorized QA personnel, with a list of authorized staff displayed at the facility entrance. Records of document access and return were maintained. The retention period for study documentation, including raw data, was defined in the SOP, specified in the sponsor–CRO contract, or required by regulations, whichever was longer. Archiving procedures were verified through successful retrieval and traceability of trial-related documents during the inspection.

5. Premises

During the inspection, a facility tour was conducted on Day 2, including the Pathology Laboratory.

The main laboratory building comprised three floors (ground level and two upper levels), each further divided. Vimta Labs Limited's Cherlapally facility, built in 1994, consisted of two buildings with a total area of 48,000 sq. ft. The facility housed Clinical Pharmacology Units with a total capacity of 180 beds for the conduct of BA/BE studies. The bed capacity was distributed as follows: CPU II – 26 beds, CPU III – 12 beds, CPU IV – 32 beds, CPU V – 54 beds, and CPU VI – 56 beds. In addition, the facility included five ICU beds in total.

The facilities were maintained in a clean condition with adequate lighting, ventilation, and environmental control. Floors, walls, and workbench surfaces were designed to be easily cleaned and decontaminated.

Clinical trials were conducted under conditions ensuring subject safety, and the site selection was appropriate to the potential risks involved.

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The CRO had sufficient space to accommodate personnel and study activities, and the trial site was equipped with adequate laboratories and equipment.

Entry to the facility was restricted and controlled through keycard access. Alarm systems were installed to detect subject exits from clinical facilities, and/or the doors were locked. All entries and exits were recorded. The list of personnel authorized to access the Deep Freezer room at the CPU was not displayed, but was provided during the inspection. The key was retained by security. The laboratory premises were designed to suit the intended operations and had two access-controlled entrances. Adequate storage space was available for samples, standards, solvents, reagents, and records.

Clinical activities included a pharmacy where investigational products were stored under appropriate conditions. Entry and exit were access-controlled, and appropriate visit records were maintained.

The laboratory premises were designed to provide adequate protection for employees and authorized external personnel, including inspectors and auditors, ensuring safety while handling or working in the presence of chemicals and biological samples.

Safety data sheets were available to staff before testing. Laboratory personnel were familiar with and knowledgeable about the material safety data sheets for the chemicals and solvents handled. Staff were trained in the use of firefighting equipment, including extinguishers, fire blankets, and gas masks, and instructed to wear laboratory coats or other protective clothing, including eye protection. Highly toxic and/or genotoxic samples were handled in a safety cabinet to minimize contamination risk. All chemical containers were fully labelled with appropriate warnings.

Adequate insulation and spark-proofing were provided for electrical wiring and equipment, including refrigerators. Rules for the safe handling of compressed gas cylinders were observed, and staff were familiar with relevant colour identification codes. Staff were aware of the requirement to avoid working alone in the laboratory. First-aid materials were available, and staff were trained in first-aid techniques, emergency care, and the use of antidotes. Containers with volatile organic solvents, such as mobile phases or extraction solvents, were sealed appropriately. Volatile organic chemicals were handled under certified fume hoods or air extractors, and safety showers and eye wash stations were available in the laboratory.

The premises had systems for waste disposal, fume treatment, and environmental protection in compliance with local or national regulations. Backup generators were also available.

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

6. Personnel

A sufficient and qualified team of medical, paramedical, technical, and clerical staff was available to support the trial and respond effectively to emergencies. Qualified and trained personnel were present at all stages, including night shifts, to safeguard subjects' rights, safety, and well-being and to provide emergency care. Contract workers were employed for specific activities to complement the team's capabilities.

The facility employed 135 staff members, with working hours from 09:00 to 18:00 and shifts ensuring 24-hour coverage. Randomly selected curricula vitae and training records of full-time and contract personnel involved in trial activities were reviewed and verified. Training was conducted in accordance with SOP for Training Procedures and Records.

Clinical section

7. Clinical phase

The clinical phase of the studies was conducted on the CRO premises.

Facilities for changing, storing clothes, washing, and toilet use were clean and adequate for the number of users. Lockable toilets were alarmed, with doors designed for external access in case of medical emergencies. Accommodation facilities were equipped with systems allowing subjects to alert CRO staff when needed.

The clinical site comprised facilities for subject registration and screening, including obtaining informed consent while ensuring privacy; the CPU; subject recreation areas; a pharmacy; sample processing and storage (e.g., plasma separation and freezers); an archive facility; and a well-organized ICU were also available. The in-house kitchen, intended for the preparation of standard meals for study subjects, was visited during the inspection. It was noted that the kitchen was not appropriately cleaned to meet the standards required for use in clinical activities. The site was strongly recommended to implement robust sanitation procedures and hygiene monitoring to ensure suitability and compliance for such use.

Vimta had an in-house digital X-ray facility and, if required, an agreement with designated hospitals to perform X-rays. Provisions were established for the urgent transportation of subjects to the respective hospitals, with corresponding service agreements available.

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Access to the randomization list was restricted to the pharmacist in charge of the study, and its distribution was documented. For each protocol, the pharmacist issued a Randomization Requisition Form to the statistician. The randomization list was generated, verified by QA, and handed over to the pharmacist for storage in the pharmacy area.

The equipment was calibrated at predefined intervals, and the function and performance of emergency-use equipment (e.g., defibrillators) were verified at appropriate intervals. Calibration certificates for the scale and stature meter were provided and reviewed.

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

8. Clinical laboratory

Vimta established a partnership with a pathology Laboratory to manage volunteer samples from BA/BE and clinical studies, with the Laboratory operating within the same facility. An agreement was signed on 30 December 2024, effective 1 January 2025. The facility and equipment used were the same as those for the studies within the scope of this inspection. Vimta Labs Ltd. provided the built-up space, utilities, furniture, and amenities such as uninterrupted power and water supply, while the Laboratory was responsible for supplying its own laboratory equipment and deploying skilled personnel to operate the pathology laboratory. At the time of the studies within the scope of inspection, Vimta used its in-house laboratory operated by the CRO. It was noted that during that period, drug and alcohol tests were performed by the laboratory; however, the practice has since changed, and such tests are now performed using applicable kits.

Hematological tests, urine analysis, and other specified tests were performed during the clinical trial in accordance with the study protocol. Sample labelling, receipt, storage, and chain of custody were maintained to ensure full traceability and integrity.

The CRO received information on the analytical methods used in the laboratory, along with a dated list of laboratory normal ranges. The current facility was certified according to ISO 15189:2022. During the study, the facility had been accredited under another certificate. The current signed curriculum vitae of the Head of the Clinical Laboratory was reviewed.

The laboratory generated individual reports for each subject, which were included in the CRFs. Source or raw data for all tests were archived in electronic and paper formats, depending on their origin and the laboratory's storage capacity. The Pathology Laboratory

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used the LIMS software system for recording results, which was reviewed during the inspection. Any change required a remark, which was reflected in the instrument audit trail. Results from sample analyses were automatically transferred to the LIMS, and the laboratory provided the Clinical Department with paper copies of the results. Data integrity requirements for all study-related tests were ensured through adequately validated systems used for sample analysis.

9. Ethics

Trials were approved by the Independent Ethics Committee prior to initiation. For the Praziquantel study, approval was granted by the Independent Ethics Committee on 7 February 2023. The committee's independence from the sponsor, investigator, and CRO was verified through the member list. The minutes of meetings documented the IEC's recommendations and decisions. The IEC was given sufficient time to review protocols, informed consent forms, and related documentation.

Insurance coverage was provided for the period 13 March 2023 to 12 March 2024. For the previous period, insurance had been provided through another Insurance Company.

Informed consent form

Information for study participants was provided in vernacular languages at a level appropriate to their understanding, both orally and in writing. For the Praziquantel study, versions were available in English (Version 01, dated 27 January 2023), Telugu (Version 01, dated 27 January 2023), and Hindi (Version 01, dated 27 January 2023).

Informed consent was obtained from each subject and documented in writing before initiation of any trial-related activities. For the Praziquantel study, informed consent was also recorded on video. The information provided made clear that participation was voluntary and that subjects had the right to withdraw from the study at any time without providing a reason. Reasons for withdrawal, when given, were documented in the study records.

Information on insurance and procedures for compensation or treatment in the event of injury or disability related to trial participation was available through the insurance policy.

Volunteers were given the opportunity to discuss potential side effects or reactions to the investigational products with a physician before participating in the trial.

The certificate of back translation of the informed consent form was reviewed.

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10. Monitoring

The Praziquantel study was monitored by monitors employed by the CRO/sponsor. Pre-study, post-study, and interim monitoring visits were conducted. Monitoring reports were provided to the site by the sponsor after each visit and were issued and addressed in a timely manner. The site initiation visit was conducted by the monitor on 22 February 2023.

11. Investigators

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

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

Information on the receipt, storage, handling, and accountability of investigational products at all stages of the trial was recorded. For the Praziquantel study, details of shipment, delivery, receipt, description, storage (including conditions), dispensing, administration, reconciliation, return, and/or destruction of remaining products were verified. Documentation included dosage form, strength, lot number, and expiry date.

Pharmaceutical products were stored under appropriate conditions in a Humidity Chamber, as specified in the official product information provided by the sponsor. Storage conditions were monitored through the digital system. The audit trail for the period 22 February 2023 to 11 April 2023 was requested and reviewed.

Randomization was conducted in accordance with the applicable SOP (Issue 9, applicable at the time of the Praziquantel study). Records, including the randomization list and seed, were maintained.

The investigational products were properly labelled. Compliance of all labels with the randomization list was verified after printing and before container labelling.

Adequate routines for labelling and documenting IMP administration were established to verify that each subject received the product dispensed for them by using labels with a tear-off portion. One label was affixed to the container, and the identical tear-off label was affixed to the CRF at the time of dosing.

Empty containers for the test and reference investigational products were labelled separately and kept segregated in a secure, locked area to prevent potential mix-ups until the dispensing stage.

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Dispensing and packaging procedures were performed in compliance with the applicable requirements, and dosing was carried out in accordance with the respective SOP.

The product handling surface was thoroughly cleaned before bringing bottles into the area. All product containers, labelling materials, contaminants, dirt, and debris were removed. A second person verified that the area was clear and clean before containers were brought in and opened. IMPs were handled with appropriate utensils, and tablets were dispensed into containers in accordance with the randomization list for the test or reference product. Test and reference products, including labelled containers, were handled at different times. Every step was recorded sequentially in detail. The handling surface and surroundings were cleared and cleaned immediately before and after dispensing each product, including within the same study.

Investigational product accountability and dispensing records were maintained, with each activity documented at the time of performance, including doses administered and returned, and verification of each step by a second person. Line clearance and accountability of retention samples of R (Praziquantel) were reviewed during the pharmacy inspection. The pharmacy was well organized, with a separate room dedicated to dispensing IMPs.

Dosing was performed in accordance with SOP for Administration of Study Medications under the supervision of the investigator and a qualified staff member explicitly delegated in writing. Doses were administered to volunteers at their beds, one by one, in several batches/teams, each consisting of four staff members with defined responsibilities. A sponsor representative was present during the inspection. Labels were checked before dosing, and the exact dosing time was documented on the designated CRF page. For solid oral dosage forms, a mouth check was conducted using a tongue depressor or spatula and a penlight to ensure the subject had swallowed the IP. Dosing was directly documented in the CRFs. Synchronized clocks were available throughout the facility to ensure accurate recording of activity times.

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 most recent product, or as specified in the sponsor–CRO contract. Dispensed but non-administered products were also retained.

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13. Case report forms

The CRFs for the Praziquantel study were randomly reviewed and verified.

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

14. Volunteers, recruitment methods

Procedures for recruiting volunteers were defined in SOP for Volunteer Recruitment and Screening Process and SOP for Volunteer Enrollment and Admission to the CPU and included a description of the methods the CRO used for this purpose. A volunteer database was maintained to avoid cross-participation and to enforce minimum intervals between studies. Access to the database was password-controlled to protect volunteer confidentiality. Identification of volunteers and subjects was ensured through a biometric system using a fingerprint reader. The biometric system was periodically validated.

Informed consent was obtained from potential subjects for screening procedures required to determine study eligibility, in addition to consent for participation in the research portion of the study. The clinical trial protocol specified inclusion and exclusion criteria and screening procedures. A software system was used to identify any prior trial participation by subjects, with participation data uploaded to a central repository to prevent over-volunteering. Access to the database was controlled.

ECG machines were used for ECG recording, with results documented on controlled-number paper. The device was designed to provide standardized 12-lead ECG measurements with automated analysis and interpretation. The technician did not have the right to modify data, ensuring data integrity. The system stored up to 200 records, after which older data were automatically overwritten.

The X-ray facility was visited. The facility was established on 14 December 2012 and received approval from the Government of India on 1 February 2023. X-ray images were recorded using a medical imaging portal for uploading X-ray images, with access granted to the technician for uploading images and to the radiologist for evaluation.

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

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15. Food and fluids

Meals were standardized, controlled, and scheduled during study days. The CRO arranged standardized meals, snacks, and drinks for study subjects through its in-house kitchen. A Form C license was issued by the Government of Telangana/FSSAI, valid from 6 January 2023 to 8 January 2026. The person in charge of operations had an agreement with the CRO and was listed as the responsible person on the FSSAI certificate.

The in-house catering facility operated in coordination with an enterprise under the required agreement, with renewal as specified therein.

The timing, duration, and quantity of food and fluids consumed were recorded. A qualified dietitian, with appropriate training and experience, designed the standardized meals.

16. Safety, adverse events, adverse event reporting

The study was planned, organized, performed, and monitored so that the safety profile was acceptable, including to the volunteers. A medical doctor was responsible for medical decisions in the case of adverse events and notifying the relevant health authorities, the sponsor, and, when applicable, the ethics committee, specifically in the case of a serious adverse event.

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.

For the Praziquantel study, an external cardiologist was present at the facility to monitor study participants until 08:00 hours post-dose on each dosing day of every period.

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Bioanalytical Section

The inspection focused on the study related to the WHO application No. NT022, including the associated validation projects. Brief spot checks were also performed for the study related to the WHO application No. HA680. More specifically, the following records and activities were investigated:

- Source documentation and raw data for validation of 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 (QCs), and subject plasma samples in analytical runs, along with the chromatograms generated from the analytical runs.
- Preparation of stock solutions, calibration standards, QCs, internal standards, and reagents.

Furthermore, chromatograms and their integration, the absence of signals in the blank samples, and the absence of any unexplained interruptions in the injected sequences were verified. The reasons for the study sample repeat analyses and all instrument failures were reviewed. The provisions and documentation of the ISRs were confirmed. The documentation and justification for the reinjection were verified and compared with the provisions.

For the review of the study documentation, adequate support was received from well-informed and transparent personnel. Access to the chromatography software systems containing the study data, including metadata, was provided to the inspectors for data review during the inspection.

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

The method development process was adequately described and documented, and the use of the internal standard was justified based on the relevant literature. A copy of the literature was available. After method development, a validation/study plan was provided as the basis for the method validation. A stable isotope-labelled internal standard was consistently used in the MS methods, and K_2EDTA was applied as an anticoagulant.

The concentrations of Praziquantel in K_2EDTA human plasma were estimated using the LC-MS/MS method. The method was validated according to the Bioanalytical Method Validation SOP.

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The method validation related to Praziquantel was performed in 2022 and was cross-validated on a different LC-MS/MS system. During the method validation, performed as per the applicable SOP, a run size evaluation was conducted to determine the batch size. A total of 154 samples of QCs and CCs were included in the evaluation, comparable in length to those expected to be used for routine analysis.

Manual integration was not permitted, in accordance with SOP for Verification of Bioanalytical Raw Data and Re-integrations of Chromatograms, Issue 11, dated 14 February 2023. The applicable SOP was updated to include the definition of the integration parameters. It was noted that the Excel sheets used during method validation were not validated and were not included in the data file. At the time of inspection, this practice was amended, and validated Excel sheets were used for the study within the scope of inspection.

The subject sample analysis of Praziquantel was carried out from 28 April 2023 to 5 June 2023, including ISRs. The study was conducted on an LC-MS/MS system using Praziquantel DII as the internal standard (ISTD). The computer-based chromatography software was used for the evaluation of chromatograms and quantitation.

Data to support the stability of the samples under the stated conditions and period of storage were available before the start of the studies, except for the long-term stability, which was performed prior to the issuance of the study reports.

The review of the entire method validation included testing of precision and accuracy (P&A), sensitivity, selectivity, matrix effect, calibration curve, autosampler carry-over, dilution integrity, stability (including freeze-thaw stability, stock solution stability, and reference standard storage stability), hemolytic effect, recovery, and reinjection reproducibility. Cross-validation was performed as required. The matrix used for the analytical method validation was the same as that of the study samples, including the use of anticoagulants.

The purchase documentation of plasma from the supplier, including receipt, storage, retrieval, preparation, and consumption of pooled plasma, was reviewed and discussed. The agreement was signed on 7 March 2021. A new Service agreement was signed on 16 March 2023. The CRO had not qualified the vendor at the time of the study; however, new practices included vendor qualification and audit.

The sample processing was documented in the respective forms.

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Each analytical run included CC standards, QC samples interspersed throughout the run, and subject samples, all processed simultaneously. The exact sequence of processing was defined and documented. All samples collected from a given subject during all trial periods were analyzed within the same run. The acceptance criteria for the analytical runs were confirmed by reviewing the analytes' retention time, the accuracy of calibration standards and quality control samples, peak integration, and IS peak areas, in accordance with SOP for Run/ Batch acceptance criteria, Issue 10.0, dated 26 August 2022. System suitability and stabilization tests were performed prior to the start of runs on each day.

Of the total 4,703 samples, 9.05% (407 samples) were subjected to Incurred Sample Reanalysis (ISR). The samples were selected at concentrations around Cmax and in the elimination phase. The acceptance criteria were clearly defined in SOP for Incurred Sample Reanalysis, Issue 12.0, effective on 26 August 2022.

The system audit trail review was carried out at the time of the studies within the scope of the inspection, and adequate training had been provided to the responsible personnel.

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

All samples were collected at the clinical facility and analyzed in the bioanalytical laboratory. Specifications of the samples (blood plasma), including sampling method, volume, and number, were defined in the clinical trial protocol and communicated to the volunteers. Collection, preparation, transport/shipping, and storage of samples were conducted in accordance with the applicable SOPs.

Actual sampling times and deviations from the prespecified schedule were recorded, and such deviations were considered in the calculation of pharmacokinetic parameters.

Labelling of collected samples was clear, ensuring correct identification and traceability. Storage conditions (e.g., freezer temperature) were controlled, monitored, and recorded throughout storage and transportation. Records of sample storage and retrieval were maintained. Samples were duplicated in aliquots, transferred, and stored separately. For the studies within the scope of inspection, samples were transferred to the BA department's Deep Freezer (DF) room immediately after aliquoting of each time point for all subjects, as no DF was available at the CPUs at that time. The CRO has since provided Deep Freezer units at –20 °C and –70 °C in the CPUs, and samples are now stored there before transfer to the main DF room near the BA laboratory.

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The rotor diameters of the centrifuges used in the study were checked, as they could affect the RPM. Slight differences were observed and discussed with the site, and it was advised to consider using the same rotor diameter to ensure that no impact occurred on sedimentation and, consequently, on the analysis of the samples. Centrifugation conditions were defined by RPM only; use of different rotor diameters may lead to inconsistent sample separation.

19. Data processing and documentation

Integration settings were science-based and fully justifiable. The smoothing factor was kept low enough not to mask potential interferences or changes in peak geometry.

The criteria for acceptance and exclusion of CC standards and QC samples, as well as batch acceptance, were clearly defined in SOP for Run/Batch Acceptance Criteria, Issue 10.0, effective on 26 August 2022.

The source data for all analytical runs included complete information from the original first evaluation of runs (containing all calibration samples), even when the analysis was repeated. The calibration range was adequately truncated. Internal standard variations were trended and considered as part of the verification of result validity.

Full audit trails were always activated on all analytical instruments before, during, and after the method validation and the studies within the scope of inspection.

All original analytical raw data (e.g., calculations, chromatograms, and their associated audit trails) were documented in a manner that ensured traceability to the sample number, equipment used, date and time of analysis, and the name(s) of the technician(s).

All audit trail files were retained, including the results table audit trail, project audit trail, and instrument audit trail. The following SOPs were available and reviewed during the inspection:

- SOP for Handling of Data, Issue 5.0, dated 25 September 2023;
- SOP for Periodic Review of Audit Trails in Analytical Laboratory, Issue 8.0, dated 18 July 2025;
- SOP for QA Audits for Clinical Studies, Issue 17.0, dated 01 August 2025.

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

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Data entry procedures, including data validation methodologies (e.g., proofreading, double data entry), were established to prevent errors.

20. Good laboratory practices

A tour of the facility was performed to verify its suitability with respect to arrangement and safety.

The general principles of Good Laboratory Practice were followed during the bioanalytical part of the BE studies, and an appropriate QA system was established.

Deep freezers for the storage of samples and refrigerators for the storage of reference standards were adequately qualified, calibrated, and maintained. A digital system was associated with the digital thermometers to detect temperature excursions. Daily monitoring and all alarm checks were documented.

For the purpose of qualification verification, the temperature mapping of a selected deep freezer was reviewed to verify the hot spot and the location of the respective sensor. The temperature mapping process was properly carried out at the time of inspection. The transfer of samples to equivalent storage units was appropriately considered during maintenance and repair.

Balances, other measuring devices, equipment, and instruments used during the conduct of a trial were periodically calibrated and verified before use to ensure fitness for their intended purpose.

The operation, use, calibration, checks, and preventive maintenance of equipment were described in the respective SOPs, and records were maintained in accordance with applicable requirements. These activities were verified through a random review of equipment used in study-related activities. Equipment and its components were labeled with the respective ID number, date of calibration, and date of next calibration. The usage of equipment was adequately documented in the analytical sheets as well as in the respective instrument logbooks. The use of HPLC columns was recorded in the designated column usage logbook.

Chemicals, reference substances, reagents, solvents, and solutions were labeled to indicate identity, purity, concentration (where applicable), expiry date, and specific storage instructions. Information concerning the source, preparation date, and stability was available on the label or in the CoA.

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Pharmacokinetic, statistical calculations and reporting section

21. Pharmacokinetic, statistical calculations

A presentation on the process of randomization, generation, and statistical analysis was provided on Day 3. The restricted access to the respective folders was demonstrated and reviewed.

The process ensured data integrity, compliance with SOPs, and systematic QA oversight throughout the clinical research biostatistics workflow.

22. Study report

Procedures were established to ensure the quality and integrity of the study report. No discrepancies were identified between the results stated in the report and the original raw data during the inspection.

The study report included the bioanalytical part of the trial, with a description of the bioanalytical method used and a report on the validation of this method. The Principal Investigator approved the clinical study reports prior to data transfer to the statistical department. The responsible staff and management also approved the bioanalytical reports. Monitoring and audit reports were available before the release of the final study report.

Miscellaneous	
Samples taken	Not applicable
Assessment of the CRO master file	The CRO Master File was provided and reviewed.
Annexes attached	Not applicable

Part 3	**Conclusion – inspection outcome**

Based on the areas inspected, the people met, and the documents reviewed and considering the findings of the inspection, including the observations listed in the Inspection Report, as well as the corrective actions taken and planned, the studies were considered to have been conducted at an acceptable level of compliance with WHO GCP/GLP/BE guidelines at ***Vimta Labs Ltd,*** located at ***142, IDA, Phase II, Cherlapally, Hyderabad 500051 Telangana, India***.

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All the non-compliances observed during the inspection that were listed in the complete report, as well as those reflected in the WHOPIR were addressed by the CRO to a satisfactory level, before the publication of the WHOPIR.

This WHOPIR will remain valid for three 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***

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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

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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