20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

Prequalification Unit - Team 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	Cliantha Research Limited, Cliantha Corporate TP 86, FP 28/1, Off S.P. Ring Road Sarkhej, Ahmedabad Gujarat 382210 India
Name and Address of Bioanalytical Research Site	Cliantha Research Limited, Cliantha Corporate TP 86, FP 28/1, Off S.P. Ring Road Sarkhej, Ahmedabad Gujarat 382210 India
Name and address Statistical Site	Cliantha Research Limited, Cliantha Corporate TP 86, FP 28/1, Off S.P. Ring Road Sarkhej, Ahmedabad Gujarat 382210 India
Corporate address of the Organization	Cliantha Research Limited, Cliantha Corporate TP 86, FP 28/1, Off S.P. Ring Road Sarkhej, Ahmedabad Gujarat 382210 India Email: nsharma@cliantha.com Website: www.cliantha.com
GPS coordinates	22.99181 N 72.47915 E
WHO product numbers covered by the inspection/ Product names/ Study numbers/ Study titles	**WHO application no. NT021** Bioequivalence study of Albendazole tablets 400 mg **WHO application no. MA196** Bioequivalence study of Primaquine phosphate tablets USP 15 mg **WHO application no. RH106**

	Bioequivalence study of the Medroxyprogesterone Acetate suspension (104 mg/0.65 ml) for injection **WHO application no. HA801 (Only clinical)** Bioequivalence study of Abacavir (sulphate) / Dolutegravir (sodium) / Lamivudine Tablet, Film-coated 600mg/50mg/300mg
Inspection details	
Dates of inspection	13-17 January 2025
Type of inspection	Routine
Introduction	
Summary of the activities	Cliantha Research is a full-service Contract Research Organization providing comprehensive and integrated offerings in Early Phase (BA-BE and Phase I), Late Phase (II-IV), Bioanalytical, Biosimilars, Nutraceutical, Dermatology, Biometrics, Cell Culture, and Consumer Research. The CRO's facilities are approved by the Drug Controller General of India (DCGI). Cliantha Research offers clinical and bioanalytical services designed to support drug development and regulatory submissions. Key offerings include: **Clinical Services:** • **Bioavailability (BA) / Bioequivalence (BE) Studies:** Conducted on healthy males, geriatric males, healthy females, and post-menopausal females. These include single and multiple-dose studies. • **Specialized Studies:** Pulmonary studies, biosimilar studies for antibodies, low molecular weight heparins, and recombinant protein-based therapeutics. • **Phase I Studies:** Conducted on small groups of healthy volunteers to evaluate safety, determine safe dosage ranges, and identify side effects. Includes SAD (Single Ascending Dose), MAD (Multiple Ascending Dose), and studies for drugs requiring complex dosing or close supervision due to high-risk potential. • **Patient-Based Studies:** Includes Bioequivalence and clinical endpoint studies, Phase II-IV studies, feasibility studies, project and site management, risk-based monitoring, investigator selection and recruitment, medical monitoring, and clinical trial supply management.

	• **Dermatology Trials:** Services include clinical trials for transdermal drug delivery systems, topicals, wear and adhesion studies, cumulative irritation studies, Human Repeat Insult Patch Studies, and other specialized skin testing procedures. **Bioanalytical Services (Small and Large Molecule):** • **Method Development and Validation:** Comprehensive method development and validation for a wide range of analytical needs. • **Study Sample Analysis:** Includes ligand-binding assays, pharmacodynamics/pharmacokinetic studies, immunogenicity studies, clot-based assays, biomarker assays, and vaccine studies. **Pharmacokinetics and Statistical Analysis:** • **Pharmacokinetic Evaluations:** Detailed analysis of drugs and their metabolites. • **Statistical Analysis:** Includes evaluations of bioequivalence and clinical trial data. • **Regulatory Reporting:** Final report compilation in eCTD format for regulatory submissions.
General information about the company and site	The organization operated facilities across six sites in India, including three in Ahmedabad (Cliantha Corporate, Arista, and Templesafe – Archive Facility), one in Vadodara, and two in Noida. In 2004, the company established its headquarters in Ahmedabad and offered clinical, bioanalytical, and statistical services. In 2007, it expanded with a 200-bed clinical facility in Vadodara, which included a clinical laboratory. Two years later, in 2009, it further grew by adding a 100-bed clinical facility in Ahmedabad (Sigma), also equipped with a clinical laboratory. In 2010, Cliantha launched patient-based studies, marking a significant milestone. The following year, in 2011, the company expanded its presence by acquiring the North American CRO, Hill Top Research, based in St. Petersburg, Florida. By 2013, a 48-bed Phase I unit was added at Hill Top Research, further strengthening its capabilities. The growth continued in 2014 with the establishment of a Bioanalytical facility in Toronto, Canada, and the acquisition of Karmic Lifesciences, a Data Management company in India. In 2017, Cliantha further expanded by adding a 117-bed clinical facility in Noida, which included a Clinical Lab, and acquiring Inflamax Research, based in Toronto, Canada.

	In 2021, the company established a new corporate facility and expanded its operations with a 101-bed clinical facility in Noida. Most recently, in 2023, Cliantha further increased its clinical bed capacity to 253 beds in Vadodara.
History	Cliantha Research was inspected by various regulatory agencies, including WHO (four times), USFDA (31 times), MHRA (three times), AGES (two times), ANSM, Spain (three times), ANVISA (two times), as well as regulatory authorities from MCC, Thailand, Malaysia, and Turkey. The detailed history of regulatory inspections was provided in Attachment I in CROMF. The company was previously inspected onsite from 25 to 29 June 2018. Additionally, a desk review was concluded on 4 January 2024. However, this specific facility was not inspected in 2018, as the CRO relocated to these premises in 2021.
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 firm 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 the 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
IB	investigator's brochure
ICF	informed consent form
ICH	International Conference on Harmonization
(I)EC	(Independent) Ethics Committee
IMP	investigational medicinal product
ISF	investigator study file
ISR	incurred sample reanalysis
IQ	installation qualification
LC-MS/MS	liquid chromatography–mass spectrometry
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
PKBS	pharmacokinetics and biostatistics
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 delivered, providing a detailed explanation of the organization's activities.

The accreditation from the Government of India with CDSCO, dated 26 February 2021, was valid for five years. An amendment was issued on 7 March 2022 to increase the number of ICU beds from 6 to 12.

The CRO had an organizational chart depicting key positions and the names of responsible persons. The chart was dated 11 November 2024, authorized, and maintained up to date.

Each employee's job description, including their responsibilities, was documented. It was randomly verified that each job description was signed and dated by the respective staff member. A confidentiality agreement for each employee was also documented. The information of randomly selected sub-investigators was verified, and their employment dates were checked in the training database for confirmation.

A list of signatures of authorized personnel performing tasks during each study was available and verified.

The principles of Good Laboratory Practices had sufficiently established the responsibilities of test facility management. The CRO management was aware that, as the investigator was an employee of the CRO, certain responsibilities typically assigned to the investigator would similarly reside with the CRO management.

Management ensured that appropriate and technically valid SOPs were implemented and followed. The maintenance of a historical file of all SOPs was adequately organized.

The Master Service Agreement (MSA) and project agreements with the sponsors were available and provided. The MSA specified that the CRO would retain samples of the test and reference products submitted by the sponsor for the duration outlined in the respective table at no charge.

The laboratory's standard working hours were from 9:00 to 18:00, with 24-hour shifts implemented as required.

2. Computer systems

A list of software and computer systems used in the studies was provided, excluding those used in the pathology laboratory. However, the list for the pathology laboratory was made available during the inspection. The software list was included as an attachment to the applicable SOP. Any changes to the network, including the temporary addition or removal of systems, were documented accordingly.

Procedures for Computer System Validation were established 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 applicable.

A sufficient number of computers were available to enable personnel to perform data entry, handle data, conduct required calculations, and compile reports. The computers possessed adequate capacity and memory for their intended use.

Access to the computer systems was protected by a combination of unique user IDs and passwords. The IT Department created access upon receiving a request from the user department. An IT application was used for raising requests, authorizing access, and deactivating or revoking user accounts. Different levels of user access were defined for each software used during study conduct. The procedures were documented in the respective SOPs.

The software programs used to perform key steps were required to be suitable and validated for their intended use. Qualification and validation certificates were provided under the user’s supervision to confirm that the software was validated for its intended

purpose and developed in a controlled manner in accordance with a QA system. The qualification of the selected systems was reviewed for verification.

The specific user requirements, regulatory and guideline requirements for BE studies, and the operating environment—including compatibility with other system components, requirement updates, user skill levels, business continuity, and upgrades—were considered in the Performance Qualification. All phases of the system life-cycle were taken into account, including concept, requirement, design, development, testing, validation, deployment, operation and maintenance, periodic review, decommissioning, and retirement.

SOPs for the usage of each software program utilized in BE study activities were available. It was ensured that access rights granted to investigator site staff aligned with delegated responsibilities and the respective tasks.

Regular updates and periodic reviews of key software programs were conducted as needed, following a risk assessment to evaluate their potential impact on current data and the qualification or validation status. These activities were carried out in accordance with SOP for System Audit, using the system audit planner. The system audit planner for 2024 was available and reviewed. Additionally, a System Audit Frequency Evaluation was conducted annually. Evidence for the year 2024, covering evaluation areas such as the BA laboratory, large molecule laboratory, biometrics, and QC laboratory, was provided and reviewed. The frequency of system audits was determined based on observations and system changes. As part of the system audit process, a system audit checklist was provided to review each system and assess whether an update was required.

All computer systems at Cliantha Research were connected to backup software and network storage devices to ensure compliance with SOP for Backup, Restore, and Rechecking of Electronic Data and Working Instructions for Backup Software. A full backup was performed on the first day of each month, while incremental backups were conducted daily. Backup data was stored on network storage, with a second copy secured on the cloud using backup software.

Procedures were established to archive electronic data from servers to separate electronic data storage and cloud storage. Firewall settings, antivirus authentication requirements, security patching, system monitoring, and penetration testing were implemented in accordance with the applicable SOPs.

The network management and monitoring system was demonstrated, and the physical location of servers was identified. A detailed flowchart illustrating the network architecture, including the full client/server structure and all relevant interfaces, was available. The flowchart incorporated several key elements related to network security, data integrity, and system control.

- A network overview was available, depicting the overall network layout.
- A client/server architecture section illustrated the client devices, such as workstations and terminals, along with their connections to servers. The data flow between clients and servers was highlighted.
- Security elements, including firewalls and access control points, were indicated.
- Additionally, a separate data flowchart was provided, detailing the main data flow and communication paths between different components, including data exchange processes between systems and interfaces.

The selected self-developed software programs were verified to be suitably validated for their intended use during the inspection.

The reliability and completeness of backups were verified through the restoration process. This was confirmed by reviewing the evidence of restoration and rechecking of electronic data backup dated 28 August 2024. The data was restored by IT and sent to the end-user for verification of readability and data integrity for the respective projects. The backup was stored on a physical server located at the site, with a copy also maintained on a cloud system in accordance with established procedures.

At the time of the conduct of the studies within the scope of inspection until February 2024, the LIMS system used in the pathology (clinical) laboratory for transferring clinical laboratory data into the database for volunteer registration and screening activities was a different software. However, as the respective vendor had discontinued support for the previous software, it was replaced by a new software system. A new volunteer and screening database was also developed to receive clinical laboratory results through the current software. Access to the volunteer database was provided during the inspection; however, previous LIMS software was no longer accessible. The respective Change control was available and reviewed.

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

3. Quality management

The Quality Management System at Cliantha Research ensured the implementation of quality standards across all projects, prioritizing data integrity and subject safety in accordance with QMS. It applied to all locations and functions, with implementation tailored to the regulatory framework of each project. The QMS was supported by procedural documents, including policies, SOPs, and plans, to strengthen compliance. It managed quality throughout all trial stages, focusing on human subject protection and the reliability of trial results, with documentation structured to support this system.

A full list of SOPs, along with the SOP documents, was provided to the inspection team on Day 1 by uploading them to a ShareDrive specifically set up for the inspection.

QA personnel were not directly involved in trial-related activities, and an in-process QA personnel audit did not replace the oversight responsibilities of other personnel when required.

The QA unit was responsible for verifying study activities, ensuring adherence to quality management systems, and confirming that protocols and SOPs were available and followed. It checked data reliability and traceability, conducted regular self-inspections, and ensured compliance with GCP and GLP, including audits of contract facilities. Additionally, it verified the accuracy of trial reports and promptly reported audit findings to management, the investigator, and the study director as applicable.

Both in-process and retrospective QA verifications, including bioanalysis checks during sample and standard preparation and testing, were conducted.

The quality management system incorporated root cause analysis, ensured all aspects of data integrity, and facilitated the implementation of appropriate corrective and preventive actions.

The company defined audit trail queries and reports for various systems and purposes in SOP for System Audit. The scope and frequency of software audits were specified in the SOP, following a risk-based approach. Key factors considered for the audit included:
- Criticality of the data generated through the software
- Duration of software implementation
- Significant changes or modifications in the software
- Significant events or incidents reported
- Major or critical observations from in-house audits or regulatory inspections

These factors were assessed before initiating an audit as part of the audit preparation and were documented in the respective checklist. For software audits, security privileges, user access rights, and audit trails related to deletion, alteration, and modification of records were verified. Randomly selected data were reviewed to identify any abnormal data patterns or modification trends.

A quarterly report was prepared by QA for their respective function and shared with management as part of the periodic review of the QMS. The report included details of quality metrics, such as ongoing issues, significant audit observations, major or critical deviations (if any), trend analysis of deviations or critical and major observations, recommendations, improvements undertaken in QMS, change management processes, external assessments from sponsor audits, regulatory inspections, and their findings, as applicable.

Change control requests were managed in accordance with the respective SOP. An example of a change control form related to the SOP on SOPs was reviewed and discussed.

Vendor audits were conducted in accordance with the respective SOP, with certificates provided on the respective form. The vendor audit for the pathology laboratory was performed in due course. The respective report and CAPA were available and reviewed.

The CRO used an application to generate unique numbers for templates used in projects, as well as general forms such as the accountability of working standards. This application had not yet been validated, as the validation process was ongoing. The risk analysis and user requirement specifications had already been provided. Until validation was completed, the issuance of templates was documented in a logbook to ensure traceability. Examples, including Reference Standards and tracking forms, were provided and reviewed.

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

4. Archive facilities

An archive facility with an approximate distance of 20 km from the Cliantha corporate. The archive was regularly audited by the CRO's auditors. The last audit took place on 19 Mar 2024, and the corresponding audit report, CAPA plan, and checklist were available for review.

According to the audit report, the archive area was access-controlled, with access restricted to archivists. The facility included a temperature- and humidity-controlled archive room, with continuous monitoring managed by the digital temperature and humidity monitoring system. Fire safety requirements were met, and evidence of pest control was available and reviewed. Work reports were available, with the last visit documented on 28 Dec 2024.

Archive activities were managed by Archival Management Software following SOP for Archival and Records Management.

Records of document access and return were maintained. The retention period for study documentation, including raw data, was defined in the SOP. This period was also specified in the contract between the sponsor and the CRO, which included provisions for the financing of archiving. According to the Master Service Agreement with the sponsor, the CRO or third-party archiving agency would retain records or study data for submission (pivotal) studies on a chargeable basis after the completion of seven years ("Free Retention Period") from the date of draft report preparation. Similarly, records or study data for non-submission (pilot) studies would be retained on a chargeable basis after one year from the date of summary report preparation.

The archiving procedures of the trial-related documentation were verified through successful retrieval and traceability of the documents during the inspection.

5. Premises

During the inspection, a tour of the facility was conducted. The laboratory was visited on Day 2.

The facilities were clean, well-lit, ventilated, and environmentally controlled, with surfaces designed for easy cleaning. Clinical trials were conducted under safe conditions, with site selection based on risk assessment. The CRO had sufficient space, laboratories, and equipment to support study activities.

Entry to the facility was restricted and controlled through biometric access, with alarm systems and locked doors ensuring subject security. Emergency evacuation measures were in place, and all entries and exits were recorded.

Clinical activity sites included two dedicated facilities as pharmacies where investigational products were stored under controlled conditions with restricted access. Entry and exit records were maintained, and the pharmacy was well organized. Two pharmacies were located on the 4th and 5th floors. The pharmacy on the 4th floor was visited, where the IP (Test product) for the study related to WHO application no. MA196 was counted and compared with the study documentation. Management oversight was effective, with logbooks available and line clearance in order. Hygienic conditions were maintained, and temperature and humidity were monitored using the digital thermometer system. The facility was mapped, with a hotspot identified for measurement.

The laboratory premises were designed to support operations effectively, with sufficient space to prevent mix-ups, contamination, and cross-contamination. Adequate storage was available for samples, standards, solvents, reagents, and records.

The facility ensured the safety of employees and authorized external personnel, including inspectors and auditors, by providing appropriate protection when handling chemicals and biological samples.

Safety data sheets were available to staff before testing. Laboratory personnel were familiar with material safety data sheets for the chemicals and solvents they handled. Staff received training in firefighting equipment use, and were instructed to wear laboratory coats, protective clothing, and eye protection. Highly toxic and genotoxic samples were handled in a safety cabinet to prevent contamination. All chemical containers were fully labeled, with prominent warnings where necessary.

Adequate insulation and spark-proofing were in place for electrical wiring and equipment, including refrigerators. Safety rules for handling compressed gas cylinders were followed, and the staff was aware of the risks of working alone in the laboratory. First-aid materials were available, and the staff was trained in first-aid techniques, emergency care, and antidotes. The training was documented in the applicable database.

Containers of volatile organic solvents, including mobile phases and liquid/liquid extraction solvents, were sealed appropriately. Volatile organic chemicals were handled under fume hoods, and safety and eye showers were available in the laboratory.

The premises had appropriate systems for waste disposal, fume treatment, and environmental protection in compliance with local or national regulations and SOP 302AK014, Version 1, for biomedical waste management.

Temperature monitoring was conducted using the digital monitoring system, which was demonstrated during the inspection.

Two backup diesel generators (750 kVA and 600 kVA) and UPS units located in a designated UPS room were available. The server room, located on the 2nd floor, was well-organized.

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 foreseeable emergencies. At all trial stages, including nighttime, trained personnel were present 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.

Randomly selected current curricula vitae and training records of full-time personnel involved in trial activities were reviewed for verification.

A software system was used to capture CVs, job descriptions, and training records, including GCP training for all employees. The system featured an audit trail, which was randomly verified. Employment start and termination dates were recorded in the system, and the inspector used it to check the revocation of access rights to the CS system.

Clinical section

7. Clinical phase

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

The studies within the scope of this inspection were conducted at the Ahmedabad Corporate facility. The Ahmedabad facility comprised eight clinics with a total capacity of 300 beds, including a dedicated 20-bed Phase I unit. It had three independent ICUs with four beds each, located on the 3rd, 4th, and 5th floors. The facility featured four independent check-in areas, a dedicated volunteer screening area, two controlled-access pharmacies, an ambulatory visit area, and two negative pressure rooms for inhalation product dosing.

Systems were in place for subjects to alert CRO staff if needed. Accommodation facilities were clean, well-organized, and sufficient for users. Lockable, alarmed toilets were designed for emergency access in CPUs. Doors were designed to allow opening from the outside in case of a medical emergency in CPUs.

The Ahmedabad facility managed a subject database of individuals for recruitment.

Provisions were in place for urgent subject transportation to the Hospital. An annual mock drill was conducted, with the last recorded on 23 Feb 2024. The time to reach the hospital was documented and found reasonable. An ambulance was available.

The equipment was calibrated at predefined intervals. The functionality and performance of emergency-use equipment, such as defibrillators, were verified at appropriate intervals.

Screening activities were conducted after volunteers signed the ICF for registration and screening. Volunteers were then registered in a database, where a unique barcode was generated to ensure proper identification and tracking throughout the screening and study process. This barcode was used for sample labeling, data entry, and subject management, enhancing traceability and minimizing errors.

8. Clinical laboratory

A suitable clinical laboratory was used for sample analysis, and it was accredited. CAP and NABL accreditation certificates were attached to the CROMF and were also available in the TMF. A backup laboratory was also contracted, and the pertaining accreditation was available. Both laboratories were accredited in accordance with ISO 15189:2012.

Haematological tests, urine analysis, and other protocol-specified tests were performed during the clinical trial.

Sample labeling, receipt, storage, and chain of custody ensured full traceability and sample integrity.

A dated list of laboratory normal ranges and the accreditation certificate of the laboratory were available in the respective TMF. APPENDIX-I of the study protocol, containing information on the Clinical Laboratory Parameters Range and Pre-defined Site Normal Range, always accompanied studies conducted for WHO applications.

The current and e-signed curricula vitae of the Head of the Clinical Laboratory were reviewed.

At the time of conduct of studies in the scope of inspection, the laboratory used PCS Lab PLUS, which was connected to the analytical instruments, allowing automatic transfer of results to the system. PCS Lab PLUS was linked to CodeLISA, providing study investigators with access to review and assess results. A PDF of the results was generated and stored in the ISF. However, the CRO had recently implemented a new LIMS, which was interfaced with all pathology laboratory instruments. The system, used for the record of clinical activities, generated barcodes for samples/vacutainers, along with analytical test requests based on the study protocol. The system used for trial activities was interfaced with the LIMS, enabling the automatic transfer of test requests. Once the samples were analyzed, the results were automatically recorded in the LIMS and then pushed into the trial software system, making them accessible to the investigator. The data recorded in the software systems was considered source data.

Data integrity requirements were ensured for all study-related tests through adequately validated systems used for sample analysis. Evidence of the interfacing of LIMS with instrument software systems was available and randomly reviewed during the inspection.

For study related to WHO application no. NT021, screening activities were directly recorded in the software system, with lab results transferred electronically from the laboratory into the respective system. However, the site also received the lab results on paper.

9. Ethics

Trials were approved by the independent ethics committee before study initiation. The committee's independence from the sponsor, investigator, and CRO was verified through the member list. Detailed meeting minutes documented discussions, recommendations, and decisions. The IEC was given sufficient time to review protocols, informed consent forms, and related documentation.

All bioavailability and bioequivalence studies were covered under the Insurance policy (Clinical Trial Liability Policy).

Informed consent form

Information for study participants was provided in vernacular languages (Hindi, Gujarati, and English) at a level appropriate to their understanding, both orally and in writing.

Informed consent was obtained from each subject and documented in writing before any trial-related activities. The information was clear, stating that participation was voluntary and that subjects had the right to withdraw at any time without providing a reason. Reasons for withdrawal were recorded in the study documentation.

Details about insurance coverage and procedures for compensation or treatment in case of injury or disability during the trial were available through the insurance policy.

The volunteers or subjects were allowed to discuss with a physician their concerns regarding potential side effects or adverse reactions from using the investigational products before participating in the trial.

The certificate of translation and back translation of the informed consent were reviewed.

10. Monitoring

The study was monitored by a sponsor representative. The monitor was appropriately qualified to ensure compliance with the protocol, GCP, GLP, and applicable ethical and regulatory requirements. This included verifying the correct procedures for completing CRFs and ensuring data accuracy.

A pre-visit and a monitoring visit were conducted during the trial. After each site visit, the monitor prepared a written report and promptly communicated any issues to the CRO and sponsor. If applicable, issues were addressed during the study to enable timely corrective action. The respective communications and corrective actions were documented.

11. Investigators

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

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

The receipt, storage, handling, and accountability of investigational products at every stage of the trial were recorded. Shipment, delivery, receipt, description, storage conditions, dispensing, administration, and reconciliation were verified. Details of the pharmaceutical products used, including dosage form, strength, lot number, and expiry date, were documented.

The following SOPs were reviewed:
- SOP for Dispensing
- SOP for Handling and storage of controlled drugs Receipt and handling of IMP
- SOP for Quarantine and release of IMP

Pharmaceutical products were stored under appropriate conditions as specified in the official product information provided by the sponsor. Storage conditions were monitored using the digital temperature monitoring system.

Randomization was performed in accordance with SOP for the Generation of Randomization Schedule. Records, including the randomization list and seed, were maintained.

The investigational products were properly labelled, and compliance with the randomization list was verified during the labelling of the containers. Labels were affixed securely to ensure the information remained intact when the lid was removed.

Adequate procedures for labelling and documenting IP administration were in place to ensure each subject received the correct product. Labels with a tear-off portion were used, with one part affixed to the container and the second attached to the CRF at the time of dosing.

The surface where the product was handled was thoroughly cleaned before bringing bottles into the area. All product containers (full or empty), individual dosage formulations, 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 using appropriate utensils. Tablets were dispensed into each container according to the randomization list for the test or comparator product. Test and reference products were handled at separate times. Every step was recorded sequentially in detail.

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, along with verification by a second person at each step.

Dosing was performed in accordance with SOP for Administration of Investigational Products to Subjects, version 2, under the supervision of the investigator and a qualified staff member explicitly delegated this task in writing. The label was checked before dosing, and the exact time of administration was documented on the designated CRF page. For solid oral dosage forms, a mouth check was conducted using a penlight to inspect under the tongue, under the lips, in the corners of the mouth, and between the gums and cheeks to ensure the subject had swallowed the investigational product. Dosing was directly documented in the CRFs.

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 and specified in the applicable SOP and the contract between the sponsor and the CRO. Dispensed products that were not administered were also retained.

An observation related to the handling of IMP was adequately addressed in the respective CAPA plan.

13. Case report forms

Randomly selected CRFs from the studies related to WHO application no. MA196 and RH106 were reviewed.

The data collected on each volunteer was specified in the trial protocol.

The lab results for screening activities for all study subjects who participated in the studies within the scope of inspection were exported from the system for review and comparison with the inclusion and exclusion criteria. The volunteer arrival record was available. The lab results for post-study tests were in paper form and included in the CRFs. The screening activities were recorded and stored in the system. The CRO currently uses a new database. Information about activities during the study was recorded in paper CRFs, and the ECGs and post-study lab results were also included in paper form.

Information about inclusion and exclusion criteria, meal distribution, dosing records, IP labels, vital signs, sample collection, urine samples for alcohol testing, and urine scans was recorded.

For transcription purposes and submission to the sponsor, the source data was transferred to another system to be converted into eCRFs. The data workflow was described in a presentation provided to the inspection team on Day 5.

14. Volunteers, recruitment methods

Registration of volunteers into the volunteer database was performed according to the applicable SOP. A database was maintained to prevent cross-participation and to specify the minimum time required between a volunteer's participation in one study and the next. Access to the database was password-controlled to secure confidential information on volunteers and subjects. Identification of volunteers and subjects was ensured through a biometric system using an "IRIS detector."

At the time of the study, another database was used for volunteer registration, but it was later replaced by the current one. Volunteer information was migrated to the new system, and a few records from the study related to WHO application MA196 were verified during the visit to the screening activities. The current database was initiated for use in February 2024.

The volunteers reported through a dedicated entry to the security office and registered in a logbook for different activities, including screening, check-in, and ambulatory visits. Their personal belongings were kept with security in the frisking room during their visit.

The informed consent of potential subjects was obtained for any screening procedures required to determine eligibility for the study, in addition to informed consent for participation in the research portion of the study. The clinical trial protocol described the criteria for subject selection (inclusion and exclusion criteria) and screening procedures. A software system, OVIS, was used to verify whether any subjects had participated in previous trials conducted by other CROs registered in the OVIS database. This system facilitated the identification of repeat participants, ensuring compliance with study eligibility criteria and regulatory requirements related to subject enrolment after the first dosing of Period I. The subjects were checked through this system at the time of check-in, using their initials and fingerprints (four fingers).

The ECG machine used for screening was connected to the registration database. The volunteer was identified by the barcode generated via this database on a wristband, and the performance of the ECG was verified in the system manually once the ECG was

scheduled. The results were printed on paper and then scanned into the system to be accessed by the cardiologist contracted by the CRO for this purpose. An application was used for the screening activities.

For x-ray procedures, a radiologist was contracted to bring a portable radiology apparatus when required and perform the x-ray. Volunteers who were required to undergo an x-ray based on the protocol typically arrived at the site before check-in for study activities, provided all other criteria were met. The image was assessed by the radiologist before the check-in procedure to ensure the subject's eligibility for study participation.

Volunteers provided urine samples, which were tested using the kits to detect the presence of narcotics and alcohol. The results of these tests were recorded and verified in the CRF. These tests were conducted prior to the check-in process to confirm that participants met the required conditions for participation in the study.

15. Food and fluids

Meals were standardized and adequately controlled, with scheduled meals during the study days. The CRO arranged standardized meals, snacks, and drinks for the study subjects as described in the clinical trial protocol, using the CRO’s kitchen, which was located 20 minutes from the site. An internal audit of the kitchen was carried out annually in accordance with the applicable SOP. The most recent report was issued on 3 May 2024. The respective internal audit reports for the past three years were available and reviewed during the inspection.

The timing, duration, and amount of food and fluids consumed were recorded. Before samples were obtained from ambulatory subjects, they were asked about their food and drink consumption. A dietitian with appropriate qualifications, training, and experience designed the standardized meals.

16. Safety, adverse events, adverse event reporting

The study was planned, organized, performed, and monitored to ensure that the safety profile was acceptable, including for the volunteers. A medical doctor was responsible for making medical decisions in the case of adverse events and for notifying the relevant health authorities, the sponsor, and, when applicable, the ethics committee, particularly 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 administered to a subject was documented and included in the CRF, along with supporting documentation in the ICU. The logbooks for medication usage in the one of ICUs (inventory log) for the period of

the study in the scope of the inspection and the usage of equipment in the ICU were reviewed.

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

Bioanalytical section

The inspection focused on studies linked to WHO application no. NT021, and MA196, including the related method validation projects. Spot checks were also performed for the study related to WHO application RH106. Specifically, the following records and activities were selectively investigated:

- Source documentation and raw data for the validation of bioanalytical methods.
- Analysis of subject plasma samples and 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 analyte 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 study sample repeat analyses and instrument failures were reviewed. The provisions and documentation of the ISRs were confirmed. The documentation and justification for the reinjection of analytical runs were verified and compared to the provisions.

For the review of study documentation, adequate support was received from well-informed and transparent personnel. The raw data in the chromatography database was made available with full administration rights to the inspectors onsite.

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

The method development process was adequately described and documented, and the usage of IS was justified. A copy of the relevant literature was available in the Pre-Method Development Work Information Sheet, where applicable. After method development, an analytical procedure (AP) was provided as the basis for method validation. A stable isotope-labelled internal standard (e.g. Albendazole D7) was consistently used in the MS methods, and an anticoagulant, e.g., K_2EDTA was applied.

During method validation as per the respective SOP, a run was performed to determine the batch with a number of QC and CC samples (so-called Analytical Run Batch Determination) comparable in length to those expected for analysis. The ruggedness validation batch also served as an extended validation batch.

The sample processing was documented in the respective forms. A note to file, i.e., a Batch Failure Form, was provided to record any unexpected activity during sample processing, where applicable.

Data supporting the stability of the samples under the stated conditions and storage period was available before the start of the studies. Long-term stability was conducted after the completion of sample analysis but before reporting.

The review of the entire method validation in both studies within the scope of this inspection included precision and accuracy testing (P&A), sensitivity, selectivity, matrix effect, calibration curve, autosampler carry-over, dilution integrity, stability (including freeze-thaw stability and stock solution), haemolytic effect, recovery, and reinjection reproducibility. Partial validation was performed in accordance with the requirements.

Some of the instruments used for Albendazole study were not part of the method validation at the time of validation. Therefore, a P&A run was performed for each instrument to replace the partial validation, following the protocol; outlined in Section 14: "All instruments used in the study should be pre-qualified with a precision and accuracy batch (including quality control samples at higher, middle, and lower levels) before study sample analysis." This requirement was specific to WHO submissions.

The matrix used for analytical method validation was the same as that of the study samples, including anticoagulants. The purchase documentation of plasma from the supplier, including receipt, storage, retrieval, preparation, and consumption of pooled plasma, was reviewed and discussed. The documentation for the reconciliation of pooled plasma, QCs, and CCs was meticulously recorded and reviewed. A random check for the usage of screened plasma in other projects was requested.

Each analytical run included calibration curve (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 analysed within the same run. The acceptance criteria for analytical runs were confirmed through a review of the analytes' retention time, the accuracy of calibration standards and quality control samples, peak integration, and IS

peak areas, as per the applicable SOPs, i.e., SOP for Sample Analysis and SOP for Sample Reanalysis (for the repeat of individual samples).

An equilibrium run (EQ), consisting of LLOQ and a System Performance Check – SPC, containing ULOQ × 6, followed by a carry-over test, was performed prior to the start of runs each day or after an interruption. Carry-over was assessed based on analyte response in blank samples following the highest calibration standard (ULOQ). The carry-over was considered acceptable if the analyte response in the blank sample did not exceed 20% of the LLOQ and 5% for the IS. The SOP also required one bulk spiking run for each study to determine the suitability of the method.

ISRs were performed in accordance with SOP for Incurred Sample Reanalysis. The respective runs were randomly checked to verify compliance with the applicable acceptance criteria.

The system audit trail review was conducted at the time of the studies within the scope of the inspection, and adequate training was provided to the responsible personnel. The QA personnel responsible for audit trail review were interviewed during the inspection, and the process was adequately explained.

Reinjection was performed in accordance with SOP for the Management of Batch Interruption/Re-injection/Continuation. A screenshot of instrument failure or notification was provided when applicable.

It was verified that plasma/serum concentration data was provided for subjects withdrawn due to an adverse event after receiving at least one dose of the study medication.

The observation related to the sample analysis (usage of plasma) has been adequately addressed in the respective CAPA plan.

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

The specification of samples (blood plasma), sampling method, volume, and the number of samples were stated in the clinical trial protocol and the information provided to volunteers. The collection, preparation, transport, transfer, and storage of samples were carried out in accordance with SOP for Handling Biological Samples After Collection to Storage, SOP for Collection of Blood Samples, and SOP for Storage, Shipment, Retention, and Disposal of Biological Samples.

The samples were received and verified by the custodian, and the receipt and transfer after study completion were recorded in a logbook for the respective Deep Freezer. Study

sample retrieval and restorage were documented on the applicable form. A separate form was used for retained samples after study completion, detailing the retrieved samples along with their verification, such as a comparison with the distribution sheet.

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

Collected samples were labelled to ensure correct identification and traceability. All storage conditions, including freezer temperature, were controlled, monitored, and recorded throughout the storage period and during transportation. Records of sample storage and retrieval were maintained. Samples were duplicated in aliquots, transferred, and stored separately.

As per SOP for Preparation of Samples in Biological Matrix, the first aliquots of study samples, QC samples, and pooled matrix were discarded. An overview of the retained samples in the archive location was provided during the inspection for all four studies within the scope of the inspection.

The sponsor's Master Service Agreement stated that biological fluids from the pivotal study were to be retained for four months after the final report was delivered to the Sponsor at no charge, while biological fluids from the pilot study were to be retained for one month after the summary report was delivered to the Sponsor at no charge. Upon completion of the specified retention period, the Sponsor was offered further options for sample disposition.

19. Data processing and documentation

The smoothing factor was kept low enough to avoid masking potential interferences and changes in peak geometry. The details of the parameters of integration settings were documented in the Analytical Procedures (AP), which were readily available to analysts. The AP also served as a template for analytical sheets.

The criteria for acceptance and exclusion of CC standards and QC samples, as well as batch acceptance, were clearly defined in the applicable SOP. The source data for all analytical runs included comprehensive information on the original first evaluation of runs, including all calibration samples, in cases where the analysis was repeated. The calibration range was appropriately truncated.

Internal standard variations (ISV) were trended and utilized as part of the verification of result validity. ISV plots were stored in the respective database. Validated Excel sheets were used for the respective calculations where applicable and were stored in the database or the study binder, as appropriate.

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

All original analytical raw data, including calculations, chromatograms, and their associated audit trails, were documented to ensure traceability to the sample number, equipment used, date and time of analysis, and the technician(s) involved. Audit trail files, such as results table audit trails, project audit trails, and instrument audit trails, were retained.

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

Data entry procedures, including data validation methods such as proofreading and double data entry, were designed to minimize errors. The data entry process was outlined in the applicable SOPs. The list of SOPs included procedures for Quality Assurance, Quality Control, Data Release, Analytical Report Preparation, Final Report Compilation, and CSR Development.

The data receipt and eCRF generation process by CDM (Central Data Management) involved multiple steps. EDC (Electronic Data Capture) training was provided to the data entry and QC clinical team, with role-based study access managed by DM. Scanned CRFs were received after QC and QA clearance and tracked by the data entry team. A single data entry process followed eCRF guidelines, with 100% source data verification by the QC team. DM conducted reviews, including null checks, dependency checks, and consistency checks, while also receiving lab datasets and reconciling them against EDC data. Queries were addressed at the site level, and responses were updated for DM, site, and QA. Medical coding (MedDRA, WHO Drug) was performed, followed by a database soft lock and an independent QA audit. After resolving queries, the database was hard-locked, and datasets were exported for statistical analysis. PDFs of the subject CRFs were then transferred to the clinic report team.

The bioanalytical laboratory to PKBS data workflow involved several steps. Study data for each run, in the form of .txt files, was transferred by the bioanalytical laboratory to the QC team and stored in a designated folder. The study data was then placed in another Drive following the applicable SOP. Using validated SAS code, QC staff generated concentration data, calibration standards, and quality control sample tables, as outlined in the respective SOP. The QC-verified tables were subsequently shared with QA for review and clearance, in accordance with the standard procedures. Once approved, the final subject concentration data was released by the QC team of the BA laboratory to PKBS in read-only mode via email, provided in password-protected Excel sheets and .xpt format for pharmacokinetic and statistical analysis following the current SOP.

The security controls for data integrity were described during the presentation provided on Day 5.

A guidance document, effective from 1 November 2023 (Version 1), was available to define the data flow for clinical conduct, bioanalytical conduct, and pharmacokinetic analysis. This guidance also covered overall study management aspects.

The ICH M10 guideline was implemented in the applicable SOPs, and a gap analysis was conducted when relevant to the studies within the scope of the inspection.

The consumption of working standards (e.g., Albendazole, its metabolite, and the IS) was recorded and checked to ensure compliance with study requirements.

20. Good laboratory practices

A tour of the facility was conducted to verify its suitability in terms of arrangement and safety.

The CRO had developed a software system that included modules designed to replace paper logbooks for refrigerators used to store stock solutions, other relevant solutions within study projects, and the usage of MS instruments. SOP for the Operation of this database, effective 8 July 2024, was available. However, the use of the application as an instrument logbook was not defined in this SOP. A change control form indicated that the Run Tracking Sheet would no longer be required after the implementation of system changes in October 2021. As a result, instrument paper logbooks were no longer applicable and were replaced by the application. Nevertheless, a maintenance logbook was still maintained for each LC-MS/MS instrument.

The general principles of Good Laboratory Practice were followed during the bioanalytical phase of the BE studies, with an established and appropriate QA system in place.

Deep freezers used for sample storage and refrigerators used for storing reference standards were adequately qualified, calibrated, and maintained. An alarm system was integrated with the digital thermometer to trigger SMS notifications and a buzzer alert to custodians responsible for facility maintenance and security. The automatic alarm system was tested during the inspection to verify its functionality. Daily monitoring and all alarm checks were documented.

For qualification/verification, the temperature mapping of two Deep Freezers was reviewed to assess the hot spot locations and the placement of the respective sensors, in accordance with SOP for the Operation, Maintenance, and Calibration of Freezers and Refrigerators. The temperature mapping process was properly conducted. During maintenance and repair, the transfer of samples to equivalent storage units was appropriately considered. The maintenance logbook of one of the DFs was reviewed. Defrosting of freezers was performed in accordance with the SOP.

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

The operation, use, calibration, checks, and preventive maintenance of equipment were described in the respective SOPs, with records maintained in accordance with applicable requirements. These activities were verified through a random review of the equipment used in study-related activities. Each piece of equipment and its components were labeled with the respective ID number, date of calibration, and next calibration due date. Equipment usage was documented in the analytical sheets, as well as in the respective instrument logbooks or electronic logbooks in the respective database. Column washing was performed by the designated column custodian using a washing system with the mobile phase after a defined number of uses, as per the applicable SOP. The periodic qualification of the following equipment was reviewed:

- 2 x LC-MS/MS instruments
- Balance – Microbalance

It was noted that one of the instruments used for the study in the scope of the inspection and its associated components was discontinued for further analysis in July 2017 and was no longer available in the laboratory. A change control was raised to document the decommissioning process. The instrument data was stored on a hard disk and retained as a backup. A total of 20 tests related to the method validation performed on this instrument were provided for inspection review.

Chemicals, reference substances, reagents, solvents, and solutions were labeled with relevant details, including identity, purity, concentration (where applicable), expiry date, and specific storage instructions. Information on the source, preparation date, and stability was available either on the label or in the Certificate of Analysis (CoA).

Pharmacokinetic, statistical calculations, and reporting section

21. Pharmacokinetic, statistical calculations

A presentation to explain the procedures and the respective data flow and data processing was provided.

A database of trial records was maintained and locked as soon as possible after the completion of the study, in accordance with SOP for Data Release (Laboratory), effective 30 Dec 2024, version 3. A Data Lock and Release Form and a Data Unlock Request and Re-release Form were attached to this SOP. Once the database was locked, the study was unblinded, and statistical analysis was performed. The locking and statistical analysis dates were documented and mentioned in the study report at the time of inspection. However, this practice had been recently implemented following a recent audit.

22. Study report

The clinical study report workflow was presented in a presentation on Day 5, outlining compliance with ICH E3 requirements. The verification steps were described, along with the investigators' approval process.

The study report included a report on the bioanalytical part of the trial, including a description of the bioanalytical method used and a report on the validation of this method. The Principal Investigator approved the clinical study reports before 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	***N/A***
Assessment of the CRO master file	Contract Research Organization Master File, dated 19 Nov 2024 was provided before the inspection and it was reviewed.
Annexes attached	***N/A***

Part 3	**Conclusion – inspection**

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 ***Cliantha Research Limited, Cliantha Corporate***, located at ***TP 86, FP 28/1, Off S.P. Ring Road, Sarkhej, Ahmedabad, Gujarat, 382210; India***.

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***

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. 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

15. 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