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**Prequalification Team Inspection services**
**WHO PUBLIC INSPECTION REPORT**
**Bio-Equivalence Study**

| **Part 1** | **General information** |
|---|---|
| **Company details** | |
| Name of Company | Accutest Research Laboratories (I) Pvt. Ltd. |
| Corporate address of Company | A-31/77, Khairane MIDC, TTC Industrial Area,<br>Khairane, Navi Mumbai-400 709<br>Ph: +91-22-2778 0718/19/21. Ext: 413<br>Mobile: +91 9833009918 |
| **Inspected site** | |
| Name and Address of the inspected site | **Clinical site**<br>**Accutest Research Laboratories (I) Pvt. Ltd**.<br>1st & 2nd Floor, Synergy Square Complex Krishna Industrial Estate,<br>BIDC, Gorwa Vadodara<br>390016, India |
| GPS coordinates | Latitude: 22,3294<br>Longitude: 73,1660 |
| **Inspection details** | |
| Dates of inspection | 16-18 January 2019 |
| Type of inspection | Initial |
| **Introduction** | |
| Brief description of the activities performed at the site | The site provided services in performing of clinical trials related to bioavailability and bioequivalence studies in Vadodara. |
| General information about the company and site | Accutest Research Laboratories (I) Pvt. Ltd. is acting as CRO providing services exclusively to pharmaceutical industry in field of formulation development and clinical research. The organization was divided in five centers in Mumbai (two units), Ahmedabad (two units) and Vadodara (one unit). There was also a Unit II in Mumbai, functioning as off-site archive facility.<br><br>The site was 29499 sq. ft. comprising first and second floor, located in Gorwa area of Vadodara. The site was only dedicated to clinical part of bioequivalence/bioavailability studies, and consisted Clinical, Quality Assurance, |

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| | Regulatory Affairs, Archiving, IT, Other Administrative & account related facilities. |
| History of previous inspections | The site was inspected by various regulatory authorities, including USFDA, ANVISA, UK MHRA, NPRA (Malaysia), MOH of Turkey and CDSCO. The site was not previously inspected by WHO. |
| **Brief report of inspection activities undertaken – Scope and Limitation** | |
| Area inspected | The scope of the inspection included a review of the following study-related activities:<br><br>The company's history, clinical study performance, informed consent process, ethics committee approvals and correspondence, test product accountability, dispensation and storage, processing and handling of plasma samples collected during the study, equipment calibration, employee training, computer controls. Tours of the facilities were also conducted. |
| Restrictions | Not applicable |
| Out of scope | Not applicable |
| WHO product numbers covered by the inspection/ Product names/ Study numbers/ Study titles / sponsor | **Study no. ARL/13/268**<br>A Randomized, Open Label, Balanced, Two-Treatment, Two-Period, Two- Sequence, Single Oral Dose, Crossover, Bioequivalence Study of Artemether and Lumefantrine Tablet 80/480 mg<br><br>**Study no. ARL/16/074 & ARL/16/075**<br>Two bioequivalent studies were conducted for the product of Dihydroartemisinin 40 mg and Piperaquine Tetraphosphate 320 mg dispersible Tablets.<br><br>**Study no. ARL/16/326 & ARL/16/325**<br>Bioequivalence studies on Dihydroartemisinin 40 mg and Piperaquine Tetraphosphate 320 mg dispersible Tablets.<br><br>**Study no. ARL/17/130**<br>A Randomized, Open Label, Balanced, Two-Treatment, Two-period, Two Sequence, Single Dose, Crossover oral Bioequivalence Study Comparing Test Product (T) Atazanavir Sulfate and Ritonavir Tablets 300 mg/100 mg |

| Abbreviations | Meaning |
|---|---|
| ADR | adverse drug reaction |
| AE | adverse event |
| ALCOA | attributable, legible, contemporaneous, original and accurate |
| 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 |
| CoA | certificate of analysis |
| CS | calibration standard |
| CSR | clinical study report |
| CSV | computerized system validation |
| ECG | electrocardiogram |
| F/T | Freeze thaw study |
| GCP | good clinical practice |
| GLP | good laboratory practice |
| HPLC | high-performance liquid chromatograph |
| HQC | high concentration quality control standard |
| IB | investigator's brochure |
| ICF | informed consent form |
| ICH | International Conference on Harmonization |
| IEC | (independent) ethics committee |
| IMP | investigational medicinal product |
| IS | internal standard |
| ISR | incurred sample reanalysis |
| ISV | internal standard response variation |
| JD | job description |
| LC-MS/MS | liquid chromatography–mass spectrometry |
| LIMS | laboratory information management system |
| LLOQ | lowest limit of quantification |
| LOD | limit of detection |
| LTS | long term stability |
| MVR | monitoring visit report |
| OQ | operational qualification |

| | |
|---|---|
| P&A | precision and accuracy |
| PIS | patient information sheet |
| PQ | performance qualification |
| QA | quality assurance |
| QCs | quality control samples |
| QM | quality manual |
| QMS | quality management system |
| RT | retention time |
| 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 |
| WS | working standard |

| **Part 2** | **Summary of the findings and comments** |
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**General section**

## 1. Organization and management

A presentation was provided by explaining the organization in detail.

The organization was founded in 1998 and expanded to the Clinical Development Services in 2008 to conduct clinical trials for complex and modified release product. Vadodara site was established in 2011 with a total area of 29499 sq. Ft with capacity of 140 beds, divided in 3 wings: Wing A, Wing B and Wing D.

The organizational chart depicting key positions and the names of responsible persons was appended to the organization master file.

Sponsor Master service agreements with sponsors were prepared in accordance with the CRO's Policy and were found satisfactory.

## 2. Computer systems

A list of software and computer systems used in the studies was provided.

SLIMS data-system was not deployed for labelling of products used for WHO-applications. Labels used for WHO-products were made in detail, using an Excel template.

Access control to different restricted areas was managed by IT after receipt of an email from HR as soon as a new employee was appointed. In the time of termination of employment, another form was submitted requesting for cancelling of access.

Electronic data were backed up at regular intervals. The reliability and completeness of these backups were verified.

Transfer of data from site to site, including the volunteer database was secured through Share Drive described in the applicable SOP.

A document for functional risk assessment report for laboratory computerized system was available, where the assessment of risks related to software aspects was documented. The risk assessment of main equipment was not part of the scope. Most of the risks were generally applicable across all the systems e.g. software failure, access control, data integrity, data tracking etc. The risks related to unauthorized system access was assessed. The scoring was based on the probability, severity and detectivity and the total score was graded as high, medium and low.

A periodic summary report for site's computerized systems was provided on 21 Dec 2017 to provide information about the site's CSV status and conclusions. Review of system validation documentation, as well as the applicable recommendation were addressed in this report.

Qualification of documentation of DMS software was provided and reviewed. The User Specification Requirements document was dated on March 2018. PQ documentation concerning URS pertaining to request and reports, approved in May 2018, and OQ documentation concerning the URS pertaining to audit trail was reviewed. The audit trail test was carried out on 21 Apr 2018 to verify that changes in master records, as well as any attempt for false login and closing out of the system after three attempts were recorded as required. The documentation was approved on April 2018.

## 3. Quality management

The CRO's Quality management was investigated to ensure that appropriate and technically valid SOPs were established and followed in a proper manner.

Organization's new CRO Master File was provided in accordance with the recent recommendation from WHO- inspection team to organize the Master File according to the WHO TRS No. 957, Annex 7.

The organization's Quality Management System consisted of:

- Quality Manual
- Quality Procedures / Policies, Protocols, SOPs, SMF, Work Instructions / Equipment Manual
- Quality Records, Source Documents, Raw Data Sheets, Instrument printouts or reports, electronic data

A list of SOPs was available. During the inspection, it was verified whether the reviewed activities were performed in accordance with the organization's SOPs and written protocols.

SOPs were centrally organized/harmonized by QA-Unit located in Navi Mumbai. Each SOP consisted of three sections for each unit (Vadodara, Ahmedabad and Mumbai). Each site was responsible for revision of their own sections. Deviations from SOPs were handled by the applicable QA-unit and maintained by the regulatory team who was responsible to carry out the trend analysis once in year to be presented for the Management review team.

SOP for Change control was reviewed and compared with the recent change control record available for 2019. Change control form was issued in the DMS data-system under supervision of QA. The SOP was applicable to activities, equipment, software, hardware and infrastructure related to different departments.

Internal audits were classified either as Planned internal audit or Unplanned internal audit in accordance with the respective SOP. QA audit plan was prepared by the QA-unit, including all details and concerning both in-process and retrospective activities such as dosing, blood collection, segregation of the blood plasma. Retrospectively, 100 % of TMF and screening documents and discontinuation data and 20 % of CRFs were revised, using a designated checklist. In addition, each unit had a QC team which reported to the Head of the unit.

A list of qualified vendors was provided.

The audit report for audit of catering service provider for 2017 and 2018 was available. The site was audited, and a report was drafted respectively on 19 Aug 2017 and 2 Aug 2018. No major or minor observations were made.

Vendor audit plans for 2017 and 2018 were reviewed. Additional information about change of the audit frequency and vendors to be audited in 2019 was documented on 6 Jun 2018.

The observation made with relation to the QMS was adequately addressed in the CAPA provided by the CRO.

## 4. Archive facilities

The archive facility was managed by two archivists and accessed by key. It was confirmed that the documents transferred to the archives were kept under adequate conditions for the appropriate duration. There was another archiving facility in the same building which was not visited.

The archive facility was equipped with steel door, fire extinguishers, smoke detector and visited by Pest control service provider. The max and min temperature and humidity in the facility were recorded in the logbook every morning.

Files were kept in racks arranged alphabetically and their overview was kept in an Excel sheet.

Logbooks were deployed to keep the record of archiving documentation and retrieval of documentation. The practice was verified by successful recall of study documentation and supporting records during the conduct of the inspection.

The observation made with relation to the archive facility was adequately addressed in the CAPA provided by the CRO.

## 5. Premises

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

The premises had sufficient space to accommodate the personnel and activities required to perform studies, located at 1st & 2nd Floor, Synergy Square Complex Krishna Industrial Estate, BIDC, Gorwa Vadodara, 390016, India since 2011.

**Clinical Pharmacological Unit**

- Wing A (having capacity of 60 beds)
- Wing B (having capacity of 36 beds)
- Wing D (having capacity of 44 beds)

The premises consisted of:

- Volunteer reception area
- Registration room
- Consent room
- Medical examination room
- ECG room
- Blood collection area
- ICU
- Canteen
- Changing room with lockers
- Administrative area
- Pharmacy
- Archive
- Cold storage
- ICF presentation area and obtaining area

The facility was clean and had adequate lighting, ventilation, and was easy to clean and decontaminate.

The facility was powered by a continuous commercial electricity supply. A set of 2 Diesel Generators (DG) were available for power generation, with a capacity of 160 KVA and 125KVA respectively. Corresponding SOP and maintenance logbook were available. Additionally, one UPS of 80 KVA was in use at the site.

Synchronized clocks were located throughout the facility to document the exact time study activities occurred.

The facility's temperature condition was monitored by Eurotherm which was connected to a mother server / monitoring station through individual sensors. Temperature monitoring of pharmacy area for the period of study was provided and reviewed.

Premises used Quantum Company for safe dispose of waste and protect the environment in conformance with local regulation. SOP for Handling of biological waste was available.

ICU

The investigators were interviewed on emergency procedures such as: intubation, use of defibrillator, oxygen cylinder and nebulizer. Maintenance logbook and proper functionality of the ICU related equipment such as defibrillator, oxygen cylinder, nebulizer, ECG and pulsoxymeter were inspected and the study staff were interviewed. The emergency medication usage record and their storage condition were verified to be carried out appropriately.

The ambulance used for transfer of study subjects to the hospital was visited.

Pharmacy

The facility located on the 2nd floor was supervised by designated pharmacists and the access was provided by keys. The pharmacy was equipped with stability chamber, refrigerator, sodium vapor lamp. The refrigerator temperature was monitored by thermo-hygrometer device which was not connected to any alarm. The stability chamber was connected to digital thermometer Eurotherm.

The pharmacy was well-organized with a separate area used for dispensing of IMP. Retained samples were separately stored. Appropriate temperature, humidity and entry/exit records were maintained in the respective logbooks.

The observation made with relation to facility was adequately addressed in the CAPA provided by the CRO.

**6. Personnel**

An organizational chart was in place across all facilities and functions involved in clinical studies. The CRO had adequate number of employees to carry out the activities as per their defined job description with adequate supervision. 101 employees on permanent contracts and 25 employees on temporary contracts were involved in site's different activities at the time of inspection.

Signed and dated job descriptions and CVs of investigators and selected personnel were presented, including a description of their responsibilities.

Annual training schedule for year 2018, together with the respective SOP and delegation list for study ARL/17/130 were available and reviewed.

A Training Matrix was provided listing each individual designation, as well as all SOPs on which they were required to be trained. The documentation was stored in their e-Training system Infinium (web-based) which was displayed during the inspection. New employees were added into the system through a robust approval procedure to be allotted a role. The system was also used for registration of CV, job description, information about the designation and any other applicable information.

The SOP for employee-training management software (E-TMS) was available describing the access rights to each role-category, with designated activity/section.

A clearance certificate was issued upon departure of the resigned employee.

The observation made with relation to personnel was adequately addressed in the CAPA provided by the CRO.

## Clinical section

### 7. Clinical phase

The clinical facility was visited. The facility was clean, well ordered, easily accessible and appropriate for the intended number of study subjects. Calibration certificates of selected instruments were reviewed. Generally, equipment used in clinical sites were calibrated by external service providers at pre-defined intervals and labelled properly. Calibration of selected equipment such as refrigerated centrifuge, as well as freezer's temperature mapping were verified. The facility was equipped with fire alarm and smoke detectors. Performance check of smoke detectors was conducted every 6 months which was properly recorded.

Labelling of study medication, monitoring check list and blood sample collection form, verification of vital signs and subjects' well-being, hygienic condition of restrooms were verified. The facility was equipped with emergency alarms so that subjects could alert CRO staff in case of need both in the CPU and toilets/shower. The alarms were randomly tested.

Delegation log, Investigators' CV, training log and job description for the study no. ARL/13/268 were verified.

Medical emergency provisions were made with Sangam hospital dated on 2 Dec 2017, for the urgent transportation of subjects to the hospital for their emergency care whenever required. On the day of initiation of each study, the facility was contacted by a designated CRO staff who delivered a letter containing information regarding check-in, dosing and check-out. Hospital confirmed the receipt of information by stamp, recipient's initial and date of receipt. The process was verified for study no. ARL/17/130 on 9 Jan 2018.

The observation made with relation to clinical phase was adequately addressed in the CAPA provided by the CRO.

**8. Clinical laboratory**

Symmers Pathcare pathology laboratory was contracted to provide the results of the required bio-sample tests. The laboratory was accredited by NABL until Sep 2020 in accordance with ISO 15189-2012, also audited by the CRO on Jun 2017.

Hematological tests, urine analysis and other tests were performed during the clinical trial as specified in the study protocol. Appendix B annexed to the protocol study no ARL/17/130 with the list of reference ranges for clinical laboratory tests with normal value and clinically accepted value was approved by the respective EC.

Individual reports were created by the laboratory for each subject and were included in the CRFs.

**9. Ethics**

The study protocols and other required documentation were approved by the independent ethics committee before the study was conducted.

SOPs for constituting IEC, procedures for confidentiality/conflict of interest agreements, procedure for selection & responsibility of independent consultants, procedure for initial review of protocol, procedure for projects submitted to expedited review, procedures for review of resubmitted protocols, procedure of compensation of subjects, procedure for continuing review of study protocols, procedure for review of SAE, procedure for site visit were available and reviewed.

DCGI approval of the CRO dated 16 May 2014 was available and verified.

**10. Monitoring**

Monitoring of study ARL/16/325 was outsourced to an independent monitoring and recorded in the respective logbooks.

Monitors' CVs and monitoring plan were verified.

**11. Investigators**

CVs, training certificates, assessments questionnaires, training log and job descriptions for the following investigators were verified.

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

Information concerning the receipt, storage, handling and accountability of IMP at every stage of the trial was properly recorded in applicable log books.

The shipment generally contained IMPs sufficient quantity required for the applicable dosing. Receipt of incomplete shipments were notified to the project manager to take the proper action. The dispensing was performed by random selection of IMP packages which were chronologically numbered upon their receipt.

Records for the shipment, the respective datalogger ID number, delivery, COA, receipt, description, storage (including storage condition), dispensing, administration, reconciliation, return and/or destruction of any remaining pharmaceutical products were reviewed for studies:

- ARL/17/130
- ARL/16/074

The labelling of IMPs was done in accordance with the applicable requirements. Dispensing of the IMPs was quality controlled by a second pharmacist and in the presence of a QA representative. The presence of QA person was documented in the entry/exit logbook. The labelling was performed in accordance with the requirements and the administration of dosing was directly recorded in the CRF. A copy of labels was kept with the CRF. Pharmacy entry/exit Logbook was reviewed.

Dispensing and packaging was performed in the pharmacy area on an appropriate surface which was cleaned and checked before dispensing. The empty containers were labelled separately for the test and the reference IMP and were segregated in the pharmacy area. Dispensing of IMP was performed in accordance with a randomization list, properly received by the pharmacist in charge. Randomization lists were generated and sent through a password protected email by statistician located in Navi Mumbai or Ahmedabad site based on a request from pharmacist, with information about protocol number, number of subjects, treatment and a copy of protocol. The latest protocol version was confirmed by IEC contact person.

Samples of the products in the original container were properly retained according to the contract with the sponsor. Dispensed products which were not administered were also retained.

The observation made with relation to the handling of investigational product was adequately addressed in the CAPA provided by the CRO.

**13. Case report forms**

Case report forms for studies ARL/13/268, ARL/16/074 and ARL/17/130 were randomly reviewed.

The observation made with relation to the case report forms was adequately addressed in the CAPA provided by the CRO.

**14. Volunteers, recruitment methods**

The CRO maintained a database of volunteers with approximately 13000 volunteers. The volunteer coordinator / registration officer was responsible for contacting the volunteers to inform them about the upcoming studies. Volunteers were registered and identified biometrically in the VPMS database customized for Vadodara facility. The visitor logs were randomly reviewed for subjects enrolled in different studies. During the screening process, all volunteers were also registered in the Security Register located at the security office.

To avoid any cross participation, 90 days eligibility was verified in OVIS database for each volunteer willing to participate in the respective study. Qualified volunteers were invited for group ICF presentation conducted by the Investigator.

Following ICF signature process, a copy of the signed ICF was provided to the volunteers. Registration officer recorded the volunteers in the database and generated a unique registration number (if new) by entering the volunteer personal details such as name and address, as well as demographic data (i.e. weight, height and BMI etc).

Volunteers underwent study specific screening procedures conducted in the medical examination area/laboratory area by the medical officer as defined by the requirements of the protocol:

- General History (including Menstrual History in case of female)
- Medical History
- Physical Examination (Vital signs, General and Systemic Examination)
- Volunteers ECG
- Blood and Urine was collected by the Phlebotomist staff for pathological investigation (Haematology, Biochemistry, Immunology, Urine Analysis and other laboratory investigations if required by the respective study protocol)
- X-ray (if required).

Those volunteers who qualified with the inclusion and exclusion criteria as described in the study protocol were invited for the check–in procedures of Period I when pre-enrolment checks were conducted such as:

- Eligibility check in OVIS & Volunteer database
- Breath Alcohol Test
- General History (including Menstrual History in case of female)
- Medical History
- Physical Examination (Vital signs, General and Systemic Examination)
- Pre-enrolment investigation (if any)

All signed ICFs V03 for study ARL/13/268, dated 28 May 2014, including records concerning date and times completed in the visitors' logbook were verified. Audio/video recording of ICF process was randomly verified.

**15. Food and fluids**

The CRO arranged for standardized meals, snacks and drinks for the study subjects by providing a menu annexed to the respective protocol which was submitted to the catering service provider along with information about date, time and number of subjects. The communication could take place either by email or personally delivered by designated staff, signed for receipt of documentation.

Documentation provided for study ARL/17/130 (fed condition) was reviewed. Records of the timing, duration and amount of food and fluids consumed were properly maintained. Standardized meals were designed by a dietitian with appropriate qualification. CV and JD of the dietician were available.

**16. Safety, adverse events, adverse event reporting**

Adverse events reporting template was used for appropriate adverse event registration. Adverse event reports were assessed and signed by designated investigator.

First aid equipment and appropriate rescue medication was available and ready for emergency use at the site. Any treatment given to a subject was documented on the form, issued for this purpose.

Report of adverse events for randomly selected studies was reviewed.

**17. Sample collection, storage and handling of biological material**

The sample collection process was verified. The specification of the plasma samples, sampling method, volume, number of the samples and actual sample collection time were documented per the applicable protocol, directly into the CRF. The activities were supervised by two designated phlebotomists and the process was verified by QA for 20 subjects during the conduct of the activity.

Labelling of collected samples were clear to ensure correct identification and traceability of each sample. Both vials and vacutainers were labelled with type of sample, study no, period no and type of drug.

Deviations from schedule time for two studies were reviewed.

Sample transfer record for period I and II of study ARL/17/130 and study ARL/16/074 was properly recorded. SOP for Blood sample shipment was reviewed.

Calibration certificate for refrigerated centrifuge, issued by Perfect utilities was reviewed. Speed, temperature and timer were calibrated in accordance with the requirements.

Haemolysed sample details for study ARL/17/130 was recorded on a respective form, with subject no, timepoint, sample ID, grade of haemolysis, and initials. Degree of haemolysis was on a chart described in SOP for Blood sample collection, processing and storage.

Logbooks for usage of centrifugation instrument and storage and retrieval of samples in Deep Freezer were reviewed and compared with the shipment documentation. 3 Deep Freezers were used for storage of sample of the studies. Samples from Period I and period II were stored separately.

The temperature log of all three deep freezers used for storage of samples in the period of Jan 2018 was checked. No temperature excursion out of acceptable range was detected.

The freezers' temperature mapping reports were also provided and reviewed. Temperature mapping was annually performed by Perfect utilities, identifying the hotspot.

Two sample-aliquots were prepared for each sample, but only one of them were sent to the BA site for analytical purposes and the other one was stored at the site as control sample.

The retention time required for bio-samples was in accordance with the agreement with the sponsors.

## 18. Data processing and documentation

The general documents included SOPs, Forms, Formats and Log Formats. The SOPs described and standardized all the important study related and general procedures to be followed across the CRO. The associated Forms, Formats and Log Formats were also developed to capture the information/data that was required to be documented.

Study Protocols, Study plans, Informed Consent Documents, Case Report Forms, Analytical Plans/Procedures and other documents that provided guidance in conduct of clinical, were available. All such documents were prepared/generated, reviewed, approved, issued, used, retrieved and retained as necessary after appropriate controlling and distribution.

All original raw data was well documented. All data related to clinical activities were documented on paper templates and logbooks, with exception to CV, JD and training documentation which were recorded in DMS. Data entry process was carried out by reporting team in Vadodara. The report was sent to QA Unit for verification.

Pre-printed bound logbooks were used to record the SOP related activities chronologically. Nevertheless, some activities were recorded in logbooks which were not appropriately bounded.

SOP for Controlling and distribution of documents was reviewed. Request for issuance of forms was sent to the QA, followed by steps detailed in the SOP to issue the forms and keep the accountability.

The observation made with relation to the data processing was adequately addressed in the CAPA provided by the CRO.

## 19. Study report

The final report was compiled in accordance with the ICH E3 guideline or applicable regulatory requirement.

QA statement provided for conduct of study ARL/17/130 was reviewed.

| **Miscellaneous** | |
|---|---|
| ***Samples taken*** | Not applicable |
| ***Assessment of the CRO master file*** | CRO MF was available. |
| ***Annexes attached*** | Not applicable |

| Part 3 | Conclusion |
|---|---|

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 study was considered to have been conducted at an acceptable level of compliance with WHO GCP guidelines at ***Accutest Research laboratories (I) Pvt. Ltd.*** located at ***1st & 2nd Floor, Synergy Square Complex Krishna Industrial Estate, BIDC, Gorwa Vadodara 390016; 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, prior to the publication of the WHOPIR.

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

| Part 4 | List of guidelines referenced in the inspection report |
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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***
   http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex09.pdf

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***
   https://www.who.int/tdr/publications/documents/gclp-web.pdf

3. Guidelines for good clinical practice for trials on pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Thirty-Fourth Report, Geneva, World Health Organization, 1995 (WHO Technical Report Series, No. 850), pp. 97–137.
   ***Short name: WHO GCP***
   http://apps.who.int/medicinedocs/en/d/Js5516e/19.11.html

4. WHO guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Fifty-Second Report, Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 9.
   ***Short name: WHO TRS 1010, Annex 9***
   https://www.who.int/medicines/areas/quality_safety/quality_assurance/TRS1010annex9.pdf?ua=1

5. 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***
   http://www.who.int/tdr/publications/documents/glp-handbook.pdf

6. 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***
   https://www.who.int/ethics/publications/9789241502948/en/

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***
   http://apps.who.int/medicinedocs/documents/s18683en/s18683en.pdf

8. 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***
   http://www.who.int/medicines/publications/44threport/en/

9. Glove use information leaflet, Patient Safety, Save lives clean your hands. Geneva, World Health Organization, 2009 (revised).
   ***Short name: Glove use information leaflet***
   http://www.who.int/gpsc/5may/Glove_Use_Information_Leaflet.pdf

10. WHO guidance on good data and record management practices. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Fiftieth Report. Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5.
***Short name: TRS 996 Annex 5*** or ***WHO GDRMP guidance***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf

11. 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***
http://apps.who.int/medicinedocs/documents/s23245en/s23245en.pdf