### Part 1: General information

#### Organization details

#### Company information

<table>
<thead>
<tr>
<th>Name and Address of Clinical Research Site inspected</th>
<th>Veeda Clinical Research; Shivalik Clinical &amp; Pharmacokinetics Facility Shivalik Plaza A, Near IIM Ambawadi Ahmedabad, 380 015 India</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Veeda Clinical Research; Vedant Clinical, Pharmacokinetics &amp; Bioanalytical Facility 2nd, 3rd &amp; 4th Floor, Vedant Complex, Nr. Y.M.C.A. Club, S.G. Highway, Vejalpur Ahmedabad, Gujarat, 380 051, India</td>
</tr>
</tbody>
</table>

| Name and Address of Bioanalytical Research Site inspected | Veeda Clinical Research; Insignia Bioanalytical Facility Rev. Sur. No. 12/1, Insignia, Corporate House, Nr. Grand Bhagvati Hotel, Sindhu Bhavan Road, S.G. Highway, Bodakdev Ahmedabad, Gujarat, 380054, India |
| Name and address of Statistical Site inspected | Veeda Clinical Research;  
Shivalik Clinical & Pharmacokinetics Facility  
Shivalik Plaza A, Near IIM  
Ambawadi  
Ahmedabad, 380 015  
India  
Veeda Clinical Research;  
Vedant Clinical, Pharmacokinetics & Bioanalytical Facility  
2nd, 3rd & 4th Floor, Vedant Complex,  
Nr. Y.M.C.A. Club, S.G. Highway,  
Vejalpur  
Ahmedabad, Gujarat, 380 051,  
India |
| Corporate address of Organization | Veeda Clinical Research  
1st, 2nd, 3rd & 4th Floor, Vedant Complex,  
Nr. Y.M.C.A. Club, S.G. Highway,  
Vejalpur  
Ahmedabad, Gujarat, 380 051,  
India  
Email: venu.madhav@veedacr.com  
Website: www.veedacr.com  
Registered address:  
Shivalik Plaza-A, Near IIM, Ambawadi, Ahmedabad – 380 015, Gujarat – India |
| GPS coordinates | Insignia:  
Latitude: 23.0421  
Longitude: 72.5101  
Shivalik:  
Latitude: 23.0285  
Longitude: 72.5427  
Vedant:  
Latitude: 23.0059  
Longitude: 72.5006 |
<p>| WHO product numbers | <strong>Study no. 17-VIN-0762</strong> |</p>
<table>
<thead>
<tr>
<th>Covered by the inspection/ Product names/ Study numbers/ Study titles</th>
<th>An open label, balanced, randomized, single-dose, two-treatment, two-sequence, two-period, crossover oral bioequivalence study of Emtricitabine and Tenofovir disoproxil fumarate tablets 200 mg/300 mg in normal, healthy, adult, human subjects under fed condition.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study no. 16-VIN-0521</strong></td>
<td>An open label, balanced, randomized, single-dose, two-treatment, two-sequence, two-period, crossover oral bioequivalence study of Darunavir 800 mg tablets in healthy, adult, human subjects under fed condition.</td>
</tr>
<tr>
<td><strong>Study no. 16-VIN-0801</strong></td>
<td>An open label, balanced, randomized, single-dose, two-treatment, three-sequence, three-period, partial replicate, crossover bioequivalence study of Ledipasvir and Sofosbuvir tablets 90 mg/400 mg in healthy, adult, human subjects under fasting condition.</td>
</tr>
<tr>
<td><strong>Study no. 14-VIN-322</strong></td>
<td>An open label, balanced, randomized, single-dose, two-treatment, two-sequence, two-period, crossover oral bioequivalence study of Tenofovir disoproxil fumarate tablets 300 mg in healthy, adult, human subjects under fasting condition.</td>
</tr>
<tr>
<td><strong>Study no. 15-VIN-022 &amp; 16-VIN-0442</strong></td>
<td>An open label, balanced, randomized, single-dose, two-treatment, three-sequence, three-period, partial replicate, reference scaled average bioequivalence, crossover bioequivalence study of Artesunate Rectal Capsules 100 mg in healthy, adult, human male subjects under fasting condition.</td>
</tr>
<tr>
<td><strong>Study no. 16-VIN-0082</strong></td>
<td>An open label, balanced, randomized, single-dose, two-treatment, two-sequence, two-period, crossover, oral bioequivalence study of Pyrazinamide Dispersible Tablets 150 mg at a dose of 450 mg (03tablets of 150 mg) in healthy, adult, human subjects under fasting condition.</td>
</tr>
</tbody>
</table>

**Inspection details**

| Dates of inspection | 15 – 26 October 2018 |

---

*Veeda Clinical Research, Ahmedabad, India-CRO*  
15-26 Oct 2018

This inspection report is the property of the WHO  
Contact: prequalinspection@who.int
<table>
<thead>
<tr>
<th>Type of inspection</th>
<th>Routine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Introduction</strong></td>
<td></td>
</tr>
<tr>
<td>Summary of the activities</td>
<td>Veeda Clinical Research Private Limited provided a full range of services in Bioavailability, Bioequivalence, Pharmacokinetics and Biostatistics and Clinical trials at Ahmedabad.</td>
</tr>
<tr>
<td>Veeda as a Contract Research Organization (CRO) provides services in late phase Clinical trials and Oncology Pharmacokinetic studies conducted on patients at Investigator sites through Clinical Operations Department based in Veeda CR Ahmedabad Office. The team of the Clinical Operations Department is responsible for client co-ordination, development and maintenance of Investigator database, feasibility evaluation, site management activities and Project Management for the studies awarded to Veeda Clinical Research.</td>
<td></td>
</tr>
<tr>
<td>General information about the company and site</td>
<td>The CRO started in 2004 and expanded the activities to Shivalik (clinical site), Insignia (bioanalytical site), Vedant (clinical site &amp; bioanalytical site) and recently to Skylar (screening facility). The CRO has closed their offices in other countries.</td>
</tr>
<tr>
<td>History</td>
<td>Since the beginning of the cooperation, approximately 2600 studies have been conducted.</td>
</tr>
<tr>
<td>The Cooperate was inspected by various regulatory authorities, including USFDA, MHRA, ANVISA, ANSM, AGES, MCC, NPCB and CDSCO. Last inspection by WHO was conducted in 2013.</td>
<td></td>
</tr>
<tr>
<td>Brief report of inspection activities undertaken</td>
<td>The scope of the inspection included a review of the following study-related activities:</td>
</tr>
<tr>
<td>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.</td>
<td></td>
</tr>
</tbody>
</table>
Regarding the analytical operations, inspection coverage was provided to confirm practices, qualifications of personnel, and procedures used during the method validations and analytical testing.

A review of the clinical study data, analytical method validation, and analytical study data including comparison of the source data and the study reports was conducted.

### Scope and limitations

| Out of scope | Not applicable |

<table>
<thead>
<tr>
<th>Abbreviations</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADR</td>
<td>adverse drug reaction</td>
</tr>
<tr>
<td>AE</td>
<td>adverse event</td>
</tr>
<tr>
<td>ALCOA</td>
<td>attributable, legible, contemporaneous, original and accurate</td>
</tr>
<tr>
<td>BE</td>
<td>bioequivalence</td>
</tr>
<tr>
<td>BDL</td>
<td>below detection limit</td>
</tr>
<tr>
<td>CAPA</td>
<td>corrective actions and preventive actions</td>
</tr>
<tr>
<td>CC</td>
<td>calibration curve</td>
</tr>
<tr>
<td>CPU</td>
<td>clinical pharmacology unit</td>
</tr>
<tr>
<td>CRA</td>
<td>clinical research associate(e)</td>
</tr>
<tr>
<td>CRF</td>
<td>(electronic) case report form</td>
</tr>
<tr>
<td>CRO</td>
<td>contract research organization</td>
</tr>
<tr>
<td>CTM</td>
<td>clinical trial manager</td>
</tr>
<tr>
<td>CoA</td>
<td>certificate of analysis</td>
</tr>
<tr>
<td>CSR</td>
<td>clinical study report</td>
</tr>
<tr>
<td>DQ</td>
<td>design qualification</td>
</tr>
<tr>
<td>ECG</td>
<td>electrocardiogram</td>
</tr>
<tr>
<td>GAMP</td>
<td>good automated manufacturing practice</td>
</tr>
<tr>
<td>GCP</td>
<td>good clinical practice</td>
</tr>
<tr>
<td>GLP</td>
<td>good laboratory practice</td>
</tr>
<tr>
<td>GMP</td>
<td>good manufacturing practice</td>
</tr>
<tr>
<td>HPLC</td>
<td>high-performance liquid chromatograph</td>
</tr>
<tr>
<td>LC-MS/MS</td>
<td>liquid chromatography–mass spectrometry</td>
</tr>
<tr>
<td>IB</td>
<td>investigator’s brochure</td>
</tr>
<tr>
<td>ICF</td>
<td>informed consent form</td>
</tr>
<tr>
<td>ICH</td>
<td>International Conference on Harmonization</td>
</tr>
<tr>
<td>(I)EC</td>
<td>(Independent) Ethics Committee</td>
</tr>
<tr>
<td>IMP</td>
<td>investigational medicinal product</td>
</tr>
<tr>
<td>IQ</td>
<td>installation qualification</td>
</tr>
<tr>
<td>LIMS</td>
<td>laboratory information management system</td>
</tr>
<tr>
<td>Acronym</td>
<td>Description</td>
</tr>
<tr>
<td>---------</td>
<td>-------------</td>
</tr>
<tr>
<td>LLOQ</td>
<td>lowest limit of quantification</td>
</tr>
<tr>
<td>LOD</td>
<td>limit of detection</td>
</tr>
<tr>
<td>MS</td>
<td>mass spectrophotometer</td>
</tr>
<tr>
<td>MVR</td>
<td>monitoring visit report</td>
</tr>
<tr>
<td>NRA</td>
<td>national regulatory agency</td>
</tr>
<tr>
<td>OQ</td>
<td>operational qualification</td>
</tr>
<tr>
<td>PIS</td>
<td>patient information sheet</td>
</tr>
<tr>
<td>PQ</td>
<td>performance qualification</td>
</tr>
<tr>
<td>PQS</td>
<td>pharmaceutical quality system</td>
</tr>
<tr>
<td>QA</td>
<td>quality assurance</td>
</tr>
<tr>
<td>QC</td>
<td>quality control</td>
</tr>
<tr>
<td>QRM</td>
<td>quality risk management</td>
</tr>
<tr>
<td>SAE</td>
<td>serious adverse event</td>
</tr>
<tr>
<td>SAR</td>
<td>serious adverse reaction</td>
</tr>
<tr>
<td>SOP</td>
<td>standard operating procedure</td>
</tr>
<tr>
<td>SUSAR</td>
<td>suspected unexpected serious adverse reaction</td>
</tr>
<tr>
<td>ULOQ</td>
<td>upper limit of quantification</td>
</tr>
<tr>
<td>URS</td>
<td>user requirements specifications</td>
</tr>
</tbody>
</table>

### Part 2  Summary of the findings and comments

#### General section

1. **Organization and management**

   A presentation was provided explaining the activities of the organization in detail.

   Veeda consisted of the following bioequivalence study centres located in Ahmedabad:

   - The Insignia facility had an approximate area of about 20 000 sq. feet spread over three floors. The facility consisted of departments to meet bioanalytical phase study requirements, quality assurance, archives and Information and Communication Technology (ICT).

   - The Shivalik facility had an approximate area of about 50 000 sq. feet spread over Shivalik A wing and B wing. The facility consisted of departments to Quality Assurance, PK/Statistical phase of BA / BE studies, ITC, and Training and Development.

   - The Vedant facility had an approximate area of about 68 000 sq. feet spread over the 1st, 2nd, 3rd and 4th floors. The facility consisted of Clinical, Bioanalytical, Clinical Operations, Pharmacovigilance, Biopharmaceutical and Project Management.

   - The Skylar facility was spread over about 7143 sq. feet. Volunteer Registration and Screening activities were provided only at this facility.
Approval of Bioavailability/Bioequivalence Study Centre (Shivalik & Insignia) of Veeda Clinical Research Pvt. Ltd. was issued by DCGI on 24 April 2017. The approval for Vedant facility was issued on 19 Jun 2017.

The Organizational chart depicting key positions and the names of responsible persons was dated 20 Sep 2018, approved by Management’s representative; Dr Venu Madhav on 21 Sep 2018.

At the BA site, the working hours was divided in two shifts, with an additional night shift when necessary. The Clinical sites had three shifts, covering morning, evening and from 4pm to the next morning. The general hours were considered from 9am to 5:30pm.

The Master agreements with the sponsors were available.

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

It was confirmed that no Windows XP was in operation.

A software system (Watson LIMS) was used for regression purposes. The records of ISTD area, analyte area and area ratio created by analytical chromatographic software were automatically transferred (imported) into the software for calculation and back calculation. They could previously prepare and directly transfer the results to WinNonlin without any manual input.

Hence by using this software system, the possibility of human errors would be minimized by eliminating exportation of the data of software, such as MassLynx, Analyst® and LabSolutions, manually to the PK-department. However, this option was not available at the time of inspection since the new version of the Phoenix could not internally communicate with the old version of the software used by the CRO. The Phoenix was updated on April 2017. Currently, a password protected Excel sheet was used for the transfer of bioanalytical results to the Pharmacokinetic-Biostatistician (PB) department.

Access control to the trial-related databases was handled by the HR and IT-department using a form for “User creation” upon the employment of staff.

SOP for Management of folder structure was reviewed for access rights to different electronic folders used by designated staff.
Backup of the electronic data was made daily, weekly, monthly and yearly. LT tapes were used to keep the incremental daily backups, weekly and monthly backups and eventually a yearly backup at the end of December each year. The yearly backups were to be stored for 15 years at the off-site archiving facility.

The CRO ensured that the data collected on the tapes remained fully readable by restoring the archived tapes every 5 years.

Operational rights of different software programs used for analytical runs were designated in groups of users in the applicable SOP.

The validation process of the software used for regression purposes was reviewed. The validation protocol and the relating report (Validation Master plan) were presented.

SOP for Computerized System Validation effective 30 Nov 2017 was reviewed. Procedures for preparation of the URS and performance qualification (PQ) documentation were included in their current procedure. The URS documentation was also used for assessment of the vendor.

SOP for usage of each software program used for BE-activities was available.

Licences for the selected software systems were reviewed.

The audit trail options used in the volunteer registration database and the validated access rights were reviewed. Any essential change to the subject’s information was performed by only the investigator.

The observations made with relation to the computerized systems were adequately addressed in the CAPA provided by the CRO.

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.

An adequate CRO Master File was provided.

A Quality Assurance program was available with designated personnel, performing audit and quality control activities in accordance with the applicable requirements.
The Quality Assurance department was responsible for establishing and maintaining the Quality Assurance systems. The Head, Quality Assurance or the designated personnel was responsible for:

- Implementation and maintenance of Quality Assurance systems in the organization
- Assurance of GXP / Regulatory compliance
- Implementation of controlling and distribution of documents
- Deviation control and change control procedures.
- Review and Approval of SOPs, Forms / Formats and Study & MV Reports
- Review of procedures and documents of Clinical, Bioanalytical, Clinical Operations, Pharmacokinetics, Statistics, Pharmacovigilance and IT departments
- Vendor qualification audits for contractual services.
- Ensuring that BA/BE and Phase-1 studies are conducted as per in-house SOPs, Protocol, GXP and other applicable regulatory requirement(s)
- Reviewing and approving audit plans audit reports generated by Quality Assurance Auditors for internal and external audits.
- Preparation and submission of periodic status reports to the management, listing major areas and seeking corrective actions.
- Overseeing the in-process audit of critical activities and retrospective audits in clinical, bioanalytical, pharmacokinetic and statistical departments.
- Ensuring the quality and consistency of audits performed by Quality Assurance department.
- Co-coordinating the compliance activities for sponsor and/or regulatory audits.

All the reviewed activities in Veeda were performed according to SOPs and written protocols prepared as per the pertinent requirements of the national and international regulatory agencies as applicable, along with specific in-house and sponsor requirements, if any.

A list of SOPs was attached to the CRO MF. The Excel sheet was maintained to document the status of the SOPs. The respective department would be notified of the required revision of the SOP in advance.

According to the applicable SOP, any unresolved issues or unacceptable audit responses would be escalated to the Head, QAD / respective department Head / Management or respective designated persons for resolution.
The following SOPs were reviewed:

- SOP for Preparation of Calibration Curve Standards and Quality Control samples effective 1 Jan 2018.
  The CRO was required to separately store 18 QC samples at each level (or either 9 sets of each level considering 2 aliquots from one set could be prepared or prepare the sets considering the required volume for 18 aliquots) along with second / other aliquot of study samples for long-term storage purposes and these samples could be used for investigation purpose (of ISR samples) or any relevant requirements.
- SOP for Management of Medical Emergence, effective 22 June 2017
- SOP for Interpretation and reporting ECG
- SOP for Clinical evaluation of laboratory parameters
- SOP for Trend Analysis, effective 25 Jun 2018 – This SOP was newly revised to implement the extensive trend analysis of deviations and address them adequately. Quarterly analysis of trends by the management was implemented in the new practice. Trend analysis was done at different levels.

The audit SOP divided the audits into internal and external audits:

Internal Audits. At Veeda, audits were conducted according to the audit program, and were segregated as per their functions and scope of the audit. The internal audits took care of all the in-house activities.

Study Audits and System / Process Audits were conducted as a part of the internal audit.

Study audits were conducted according to a predefined study audit plan. The study audit included in-process and retrospective phases.

The in-process audit was carried out by QA during the actual conduct of the study in which the key activities were witnessed, whereas in the retrospective audit, the data / documents were audited as per the plan after the conduct of a study phase was completed. The study protocol / plan, SOPs and the related governing documents provided a set of standards to adhere to, apart from other mandatory norms. After auditing these activities, an audit report was prepared and sent to the respective department or personnel for rectification of the findings. Unresolved findings were escalated to Management.
System / process audits were also conducted. These audits were general in nature, non-study specific and were devised to monitor and evaluate the strength of the entire system (including facilities, equipment, and personnel) to be in accordance with the stipulated norms as laid down by in-house procedures, national and international regulations. These were carried out at predefined frequency in a calendar year for each of the systems / processes depending on the criticality of the same. After the audit, an audit report was prepared and sent to the respective department or personnel for rectification of the findings.

External audits were also carried out to evaluate the level of desired competency of an externally outsourced agency, and the quality systems prevailing in the same and to assess the quality aspects like documentation, compliance to applicable regulatory guidelines and current industry standards. The external audit was carried out as per predefined frequency and annual audit plan and includes a visit to the agency.

SOP for Audit program 12 Jul 2017 was reviewed.

The Catering audit report for catering services on Aug and Sep 2018 was reviewed. It was verified that the catering service had the necessary certifications, issued by FSSAI and Food and Drug control accreditation.

A list of studies for the last two years was provided for inspectors’ review.

A draft of new Quality policy was presented.

The observations made with relation to the QMS were adequately addressed in the CAPA provided by the CRO.

4. Archive facilities
The archive facility in both BA and clinical sites was managed by an archivist. It was confirmed that the documents transferred to the archives were kept under adequate conditions for the appropriate duration.

The archiving SOP was provided.

The archiving facility was appropriately secured with enough storage space for the documentation archived. The facility was equipped with a certified fireproof door. The humidity and temperature were measured daily, recording both min and max temperature. A monthly pest-control was carried out. Cleaning staff were supervised. The visits of the pest-control and cleaning staff were properly documented in the entrance logbook.
SOP for Management of archive effective 30 Apr 2018 was reviewed.

Folders were correctly arranged based on the receipt of the project.

The retrieval of the documentation after the inspection request was reviewed. The archive processes were tested by the successful recall of study documentation and supporting records during the conduct of the inspection.

The agreement with the off-site archiving facility; in Ahmedabad dated 5 Apr 2018 (Extended the agreement for storage of Media Tape) was reviewed. Veeda adequately audited the facility on 6 April 2018.

An Excel sheet providing an overview of the documentation archived in the facility was maintained by the archivist, with read-only access to everybody else.

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

A List of personnel with authorized access to the restricted area was available at the entrance of each facility.

The facility was powered by a continuous commercial electricity supply wherein the outages are relatively rare. There was also a Diesel Generator (DG) set for power generation and the respective SOP was available.

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

The temperature recording system was a 24-hour temperature monitoring device/recorder. Resistance Temperature Detector (RTD) probes were placed at various specified locations of deep freezers and refrigerators within the facility.
**Insignia site:**
The premises had sufficient space to accommodate the personnel and activities required to perform studies:

- LC/MS/MS Rooms
- LIMS Operators and Report Writing Area
- Bioanalytical Quality Monitor Area
- Laboratory management Area
- Sample Preparation Area
- Light Sensitive area
- High End Processing Area
- Fume hood area
- Washing area
- Deep freezer (Sample storage) room
- Balance room
- Documentation area
- Change room
- Chemical store
- Utility Room
- Electric Room

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

Entry to the CRO and archiving facility was adequately restricted and recorded. However, the entry to the other parts of the facility although restricted was not recorded in a logbook. The facilities were accessed by a key-card issued by IT-department.

Volatile organic chemicals were handled under fume-hoods.

**Skylar facility**
Since May 2018, the full registration and screening related activities were done at the Skylar facility which had an area of 7143 sq. feet. This facility was divided into registration, counselling, clinical examination, ECG, phlebotomy, urine collection and document store areas for better and efficient operations.

**Shivalik facility**
The Clinical Research Department (CRD) at the Shivalik facility was divided into six clinical housing and investigational areas on three floors (2nd, 3rd and 4th floor).
**Vedant facility**

The Clinical Research Department (CRD) at the Vedant facility was spread over total area of about 17,060 sq. feet and was divided into four clinical housing and investigational areas on two floors (2nd and 3rd floor).

Vedant also housed a bioanalytical laboratory on the 1st floor, whereas the clinics were on 2nd and 3rd floors. The 4th floor was reserved for administrative activities, server room, archives and various corporate functions. In addition, an ambulatory blood collection facility was on the -2 basement for post-study blood collection.

The Clinical facilities consisted of:

1. Change rooms (For changing into ward uniform)
2. Subjects housing (Clinical ward)
3. Special / Intensive Care Unit (ICU)
4. Doctors, Nurses and attending staff
5. Phlebotomy
6. Sample processing and Storage
7. Dining
8. Clinical examination and vitals
9. Recreational activity
10. Documentation and monitoring
11. Separate toilets and showers

The clinical facilities were equipped with major equipment such as Airpac Laminar, Humidity Chamber, walk-in chamber, Refrigerated Centrifuge, Deep Freezer, Defibrillator, Electrocardiograph, Suction Machine, Weighing balance and temperature monitoring system (Eurotherm) for continuous monitoring of temperature of refrigerator and freezers.

The sites were powered by a continuous commercial electricity supply wherein the outages are relatively rare. Uninterrupted Power Supply (UPS) took over in the event of a power failure. There was also a Diesel Generator (DG) set for power generation.

Disposal of waste and other environment-friendly measures were explained.

The ECG machine on the 3rd floor of the Shivalik site was functioning properly and storage of ECG results was not possible. This option was not available as the required diskette had not been purchased.
The entrance and exit visitor log was provided. The volunteers’ bio-samples were placed in a cooler-bag which was not appropriately closed to maintain the required temperature. However, the revision of the visit-log revealed that the samples were collected by the Clinical laboratory personnel three times on 23 Oct 2018, with one collection outstanding/imminent.

**ICU**
Each CPU had an adjacent ICU. The ICU was adequately organized, equipped, and had knowledgeable personnel and proper logbooks for usage of the equipment and medication accountability.

The ICU adjacent to the CPU-1 was visited. The ICU temperature was monitored and logged daily.

**Pharmacy**
The Pharmacy area was designed to store and dispense the Investigational Products. There were two Pharmacy areas at the Shivalik facility- one on the 3rd floor (A wing) for solid oral dosage forms and the other on the 4th floor (A wing) for suspensions. The Pharmacy area was access-controlled by key card and equipped with Pharmaceutical refrigerator, humidity chambers, walk in type chambers for storage of retained IMPs and laminar air flow bench.

The observations made related to this section were adequately addressed in the CAPA provided by the CRO.

6. **Personnel**
The CRO had approximately 900 (600 + 300) permanent and contractual employees for timely and proper conduct of the study. A list of manpower in details was provided in their Quality Manual. The records of the qualifications, training and experience for each professional was kept either individually or as a training list if group-training was provided.

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

A list of signatures of the authorized personnel performing tasks during each study was kept with the study binder, with their initials for identification purposes.

The SOP for training was reviewed.
A document consisting of 6 modules and a section for regulatory awareness with the details including the name of the SOPs belonging to the respective module was available. This list was linked to the training matrix, arranged by job title category and modules. The company also provided a list of manpower details with the name of staff, functional designation, qualification and total experience. The list was recently approved on 20 Sep 2018.

Randomly selected training documentation of SOP was reviewed.

Termination of employment was described in the SOP for Administration of User Account effective 8 Oct 2018. Termination of employment of one of the staff on 5 Oct 2018 was confirmed to be in accordance with the applicable SOP.

**Clinical section**

7. Clinical phase

**Shivalik site:**

The facility was clean, well ordered, easily accessible and appropriate for the intended number of study subjects. Equipment used in clinical sites were calibrated by external service providers at pre-defined intervals and labelled properly. The adequate function and performance of emergency-use equipment was verified prior to the initiation of the study.

The site consisted of six CPUs with sufficient space for 182 + 7 special care beds to accommodate the study subjects. The CPUs allowed supervision by the custodians during check-in periods and monitoring of subjects by CCTV. Hence, restriction of the intake of food or medication within the number of hours specified in the protocol was assured.

The facility was equipped with an emergency alarms at each bed which were randomly tested both in the CPU and in the showers. Clothing kits were placed in the changing room and lockers for storage of subjects’ personal items were provided.

The ambulance was present and labelled as such. Medical emergency agreements with the hospital for the period of the studies in the scope of the inspection respectively for both Shivalik and Vedant sites were provided.

Selected trial documentation was reviewed and verified during the inspection of the clinical phases to include various aspects of the trial.

The observations made related to this section were adequately addressed in the CAPA provided by the CRO.
8. Clinical laboratory

**Clinical/Pathology lab**

These services were outsourced to external pathology laboratory which was NABL and CAP accredited lab. CEO/Laboratory director’s CV was available.

SOP for clinical evaluation of lab parameters, effective 14 Sept 2017 was provided. The list of acceptable ranges for laboratory parameters was provided and implemented in their practice, based on three literatures given in the SOP.

The laboratory results were sent to the screening staff in the sealed envelopes, in paper.

9. Ethics

The CRO had agreements with three ethics Committees which were constituted as per the guidelines laid down by ICH-GCP E6 R2 and Indian Council for Medical Research (ICMR).

The general screening ICF as an SOP was approved on 26 Feb 2018 by all three IECs.

1. Anshan - IEC
2. Conscience - IEC
3. Sangini Hospital-IRB

The composition of the member-lists was verified. All three Ethics committee were constituted of medical, scientific and non-scientific members as prescribed by the applicable guidelines.

The insurance provided by National Insurance Company was previously limited to 300 – 350 studies per year. However, the current insurance policy schedule was changed to be applicable for 500 studies / 15 000 subjects annually.

10. Monitoring

Monitoring was performed by both the sponsors’ monitors and Veeda’s CQM-QC team.

The monitoring reports performed by the sponsors’ representatives for study no 15-VIN-022 and study no. 16-VIN-0082 and the pertaining visitor logbooks were reviewed and verified.

11. Investigators

The CVs and training documentation as well as the GCP certificates for PIs involved in the studies 16-VIN -0801 and 16-VIN-0762 were provided. Their JDs were also reviewed. Both PIs had left the CRO.
12. Receiving, storage and handling of investigational drug products

A pharmacy activity plan was provided weekly.

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 20 – 50% greater than the quantity required for the applicable dosing. Incomplete shipments were quarantined until the problem was resolved. The dispensing was performed by random selection of IMP-packages which were chronologically numbered on receipt.

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 labelling was performed in accordance with the requirements and the administration of dosing and was directly recorded in the CRF. The tear-off portion of labels was pasted onto the CRF.

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.

Samples of the products in the original container were properly retained in the walk-in chamber and according to the contract with the sponsor. Dispensed products which were not administered were also retained.
13. Case report forms

Case report forms were randomly reviewed for studies 16-VIN-0521, 16-VIN-0762, 16-VIN-0801 regarding lab-results, ECGs and deviations of blood sample collection times.

14. Volunteers, recruitment methods

Veeda maintained a database of volunteers, from which suitable volunteers for studies based on the requirements of the study, were selected. Volunteers were informed by word of mouth and reported to the facility. Volunteers were registered in the volunteer database after their eligibility was verified using the OVIS database, and after completing the screening ICF and providing impressions of both indicator-fingers and thumbs. Each volunteer thus enrolled into the database was assigned a unique identity number and was issued an identity card for having registered. This served as the proof of identity for that volunteer for all his/her subsequent visits and participation. The registration and screening history of the volunteers were tracked by the software system.

Volunteers were informed of the objective and procedures of the study and consent was obtained for screening of the volunteers. Volunteers underwent clinical examination, ECG and screening for various parameters of haematology, biochemistry, urinalysis and serological tests for HIV, HCV as defined by the requirements of the protocol or the screening physician.

The OVIS (Online Volunteer Information System) database was linked with several other bioequivalence centres to avoid cross participation by subjects.

The Chest X-ray screening activities were outsourced. The volunteers were driven to the facility in groups of 8-10 in the CRO’s vehicle after completion of other screening activities.

At the clinical sites, volunteers who participated in the screening phase were invited to report on the day of check-in of the respective study in case of eligibility or if the results were not yet available. Non-eligible volunteers were informed and handled according to the CRO’s procedures.

Those volunteers who qualified with the inclusion and exclusion criteria as described in the study protocol were considered for enrolment and required to complete the screening activities prior to the check-in. The screening activities at the clinical site consisted of OVIS-verification, Alcohol breath analysis test, urine test for drug and final physical examination including ECG.
The objectives of the study, nature and possible adverse effects of the drug, restrictions, sampling schedules and compensation for participation in the study in a language comfortable to the prospective subject were explained to the volunteers in a group. They were then required to give their consent by signing the Informed Consent Document (ICD). Audio Video recording of Informed Consent Process was performed. Consent for the study was taken by the Investigator on a one to one basis and ICD obtaining was recorded. The volunteers were then admitted for housing to undergo the study procedure.

The results of subject screening and of trial participation were recorded in adequate Case Report forms.

Medical records were generated for each subject and included information obtained during each screening visit and from each study in which the subject had participated.

The observations made related to this section were adequately addressed in the CAPA provided by the CRO.

15. Food and fluids
A kitchen facility used for preparation of veg-food for volunteers was located on the fourth floor of the Shivalik site. The facility was inspected.

The CV of the dietician was provided, and she was interviewed. The food plan was provided according to the protocol and regulatory requirements. The Plan was given to the catering service provider who was responsible for preparation of non-veg food.

The observations made related to the food preparation were adequately addressed in the CAPA provided by the CRO.

16. Safety, adverse events, adverse event reporting
Adverse events were adequately documented in the Adverse Event Reporting form according to the applicable SOP for both adverse events occurring during the study and post-study.

No SAE was recorded for any of the studies in the scope of inspection.

Concomitant medication was also captured on the same form if necessary.
Bioanalytical section

The inspection included auditing of source documentation and raw data for validation of bioanalytical methods, and analysis of subject plasma samples as well as audit of the electronic data, audit trails for electronic data capture and handling related to the PK study. Results of calibration standards, quality control samples (QCs), subject plasma samples in analytical runs were verified along with the chromatograms generated from analytical runs. The preparation of analyte stock solutions, calibration standards, QCs and internal standards, and reagents were also audited.

QA-personnel assisting the inspection team with review of study-documents were knowledgeable, transparent and helpful.

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

It was confirmed that selective and sensitive Bioanalytical methods for the quantitative estimation of drug(s) and / or metabolite(s) were developed using High Performance Liquid Chromatography (HPLC), Ultra High-Performance Liquid Chromatography (UHPLC) and LC/MS/MS techniques for each study in the scope of inspection. The methods were optimized up to the minimum quantifiable concentration (Lower Limit of Quantification-LLOQ) of the drug and / or metabolite in the plasma matrix which were generally 20-fold less than the reported / expected Cmax values. The linearity of the methods was established in the concentration range from LLOQ to a value greater than expected Cmax (at least two-fold the value of reported / expected Cmax). The Method developments were carried out to optimize extraction, chromatographic and spectrometric conditions to achieve the desired quantitation outcome followed by pre-method validation activity. The procedures were performed according to the in-house SOP for Bioanalytical Method Development. Bioanalytical method validations were carried out by using LC-MS/MS method according to the regulatory requirement and the in-house SOP for Bioanalytical method validation.

Extracts from reference literature were ‘Sellotaped’ into the method development notebooks and the method development was well-documented. Perusal of one of the oldest notebooks confirmed that the use of ‘Sellotape’ was adequately permanent.

A software system was in use to identify the potential samples for Incurred Samples Re-analysis (ISR) and the balance of the required number of samples and the related randomization was provided by the SAS software.
Back calculation of the concentrations was made by the same software by which the system identified the unacceptable analytical results in relation to the Calibration curves, concentrations above ULOQ and concentrations below the quantifiable limits. These sample results were highlighted by the software on the report.

Other batch acceptance criteria, such as ISTD variation, baseline value, etc were assessed by the project-lead using a validated Excel sheet.

**Study no. 16-VIN-0521**

After ensuring a 10-hour overnight supervised fasting before the scheduled time of intake of a high-fat high-calorie breakfast, subjects were dosed with Darunavir 800 mg tablet along with Ritonavir 100 mg tablet on Day 1 in both the periods. Ritonavir 100 mg tablets were administered twice daily (i.e. morning and evening time) on Day -2 and Day-1 (two days prior to dosing of Investigational product), Day 1, 2 and Day 3 in each of the two periods. The morning dose of Ritonavir 100 mg tablet was administered 30 minutes after the distribution of the normal breakfast (Except Day 01 morning dose) and evening dose of Ritonavir 100 mg tablet was administered 30 minutes after the start time of dinner, according to the applicable protocol.

All the stability tests were repeated in May 2016 to establish the stability of the analyte in the presence of the analyte.

The suitability of the method validation was supported by evaluation of various aspects in accordance with applicable guidelines.

The analyte analysed in this study was Darunavir, using Darunavir-D9 as ISTD. Human plasma K3EDTA was provided. The samples were analysed by UPLC-ESI-MS/MS, using MassLynx software.

The original method validation was performed on 3 – 10 May 2010, to which 11 amendments were made during the study. The details of amendments were given in the presentation provided at the opening meeting.

The results of the method validation were available before the initiation of the study, with exception to the evaluation of the long-term stability data of the analyte in the matrix.
Method validation;  Amendment 9
Start date:   23 Oct 2017
End date:   24 Oct 2017
Report date:  31 Oct 2017

Analytical runs
Start date:   17 Jan 2018
End date:   25 Jan 2018

Amendment 10 and 11 were implemented after the completion of the study. Amendment 10 was performed to assess the presence of concomitant medication, including Atropine, Oxetacine and Furazolidone. Amendment 11 was made due to an observation from NPRA to perform short-term stock solution and working solution stability testing specifically recorded as such.

Instruments used in the method validation and during sample analysis were verified.

Results and documentation pertaining to Matrix effect by evaluation of matrix factor using 10 lots provided by the clinical laboratory together with lipemic samples and haemolyzed samples (in-house), Short-term stability of stock and working solutions (aqueous), Bench Top stability followed by the Dry extract stability, Wet extraction stability and autosampler stability, Freeze – Thaw for -15 -25 °C, Freeze-Thaw for -70 - -86 °C and the long-term stability of analyte in matrix in presence of the Ritonavir in two concentrations (2 µg and 7.5 ng) based on the recommendation from the sponsor, were reviewed.

The stability of the samples from the time they were retrieved from the freezer by the time they were placed into the autosampler and further by the time that they started the analytical run was covered by various stability tests to ensure the stability of the samples during the study. The long-term stability time covered the whole period between collection of the blood samples and the last analytical run.

Purchase and usage of Ritonavir working standard was confirmed.

The system suitability runs were verified for both instruments numbers 10 and 11. The acquisition times of the samples were randomly checked and verified against system the audit trail. ISTD variation was calculated on a validated excel sheet and provided. The calculation was randomly verified. The Acceptance Criteria for the result of the sample was if the ISTD area was greater than 50 % or less than 150 % of mean ISTD area of the accepted samples.
One set of CCs and QCs were used in each run. Each CC aliquot or QC was prepared in a quantity that was enough to be used for each run. A reconciliation list of number of CCs and QCs used versus remaining was presented as a part of the study documentation which was verified. Out of 36 sets of CC and QCs, 9 sets + 1 set for (MQ method qualification) remained. In addition, 9 sets of QCs were prepared to be kept with the Aliquot 2 for future use if required upon request for re-analysis for instance for inspection purposes. The remaining QCs and CCs were all discarded with aliquot I on 25 Feb 2018 from DF with ID no 18, with exception of the 9 sets kept with aliquot 2 which were retrieved and verified from DF with ID no. 02. The applicable SOP was reviewed.

One set of CCs was used at the start of each analytical run, and the replicate of the same set was used at the end of the run. QCs were interspersed between the samples in the run.

Chromatograms and pertaining iteration parameters were also verified for randomly selected runs.

The complete information regarding the analytical runs and the relating audit trails were provided.

The sample processing procedure, storage and retrieval of the samples, as well as Watson LIMS request and result were reviewed for randomly selected runs.

The ISR runs were carried out according to the applicable SOP. The list of the samples to be used for ISR experiment was provided using Watson LIMS database.

**Study no 17-VIN-0762 and 16-VIN-0801**

The method development, method validation, and analytical runs documentation of these studies were extensively reviewed.

A comprehensive description of the bioanalytical method development was provided for both studies. Up-to-date guidelines at the time of the studies were followed.

Method validations were completed before the analysis of the study samples and the data supported the suitability of the methods.

Every analytical run reviewed included the required calibration curve and QC samples in the same run and all were adequately documented. The carry-over effect was adequately addressed. System suitability and performance was regularly run.

All events during the analyses were investigated, resolved and adequately documented.
All the repeat analyses were done according to the applicable procedure, documenting the pertaining investigation for the reason for the repeats.

The review of the audit trails on the MS/MS instruments used for the studies and other MS/MS instruments available at the time of sample analyses, verified that there were no time gaps between the runs and that relevant runs had not been performed on instruments other than those indicated.

**Study no. 15-VIN-022**

The events occurring during the study 15-VIN-022 were reviewed. These were investigated, resolved and well-documented.

All the repeat analyses were done according to the applicable procedure, documenting the pertaining investigation for the reason for the repeats.

The review of the audit trails on the MS/MS instruments used for the studies and other MS/MS instruments available at the time of sample analyses, verified that there were no time gaps between the runs and that relevant runs had not been performed on instruments other than those indicated.

The study audit trail in Watson™ LIMS was exported to an Excel sheet and reviewed. The unlocking and locking of study data was inspected. The study was locked on 16 Dec 2015. The review of audit trail did not reveal any modification to the data prior or after the completion of the study on November 28, 2015. The analytical data was sent to the PB as a pwo-link via an email.

The study was repeated, and results were presented as study no 16-VIN-0442.

The observations made related to this section were adequately addressed in the CAPA provided by the CRO.

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

The collection of samples was observed by the inspection team. The sample collection trollies were moved to the subjects in a prescribed timely manner.

The specification of the plasma samples, sampling method, volume and number of the samples were documented per the applicable protocol.

SOP for subject sample management was reviewed to verify the procedures for collection, preparation, shipping and storage of the samples.
Actual sampling times were recorded, and the deviations were noted in the study documentation.

Labelling of collected samples was clear and vacutainers were prelabelled with all the required information for identification and traceability of individual samples.

Samples were transferred to the sample processing room in ice buckets/trays and were stored in -25 and -78 ºC deep freezers available in the room, after centrifugation. The centrifugation activity was recorded in the logbook for the usage of instrument, together with applicable instruction. Haemolysis of the samples was identified and classified against the chart and recorded properly in the respective study specific form. Aliquots were distinguished by label colour.

The shipment of the samples from the clinical site to the bioanalytical site was carried out under controlled condition using temperature recording during shipment as specified in the protocol.

Labelling on the storage boxes, the sample IDs, number of samples, missing and haemolyzed, timepoints and such were verified against the shipment documentation before the samples were stored in the deep freezers in accordance with the protocol requirements.

The two sample-aliquots were shipped separately for each period. Different aliquots were stored separately in different Deep freezers.

The retention time required for bio-samples and the discarding of the samples were verified.

19. Data processing and documentation

The general documents included SOPs, Forms, Formats and Log Formats. The 350 plus SOPs described and standardized all the important study-related and general procedures to be followed across Veeda, Ahmedabad. 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, bioanalytical, statistical and other phases of study were available. All such documents were prepared/generated, reviewed, approved, issued, used, retrieved and retained as necessary after appropriate controlling and distribution.

All original analytical raw data was well-documented. Repeats and events were properly recorded and resolved and the reasons for repeats were provided in an investigation report.
Pre-printed properly bound logbooks were used to record the SOP-related activities chronologically. The unused logbooks were returned to the QA for further processing.

SOP for Controlling and distribution of documents effective 14 Jul 2018 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 issuance history of form I63 used to report the repair of the solvent evaporator was traced to verify the issuance of the templates and forms.

20. Good laboratory practices

The Insignia bioanalytical facility had 33 LC-MS/MS, as well as ECLIA, Plate Reader, ICP-OES, sample processing equipment such as refrigerated centrifuge, solid phase and liquid-liquid extraction assembly, evaporators, freezers of different ranges (-20 °C to -70 °C) for sample storage, temperature monitoring system for continuous monitoring of temperature of refrigerator and freezers, pH Meter, analytical balance and Millipore Water Purification System.

The Insignia facility had two Deep freezer rooms on the 1st and 2nd floors equipped with 20 x -80 °C Deep freezers, 6 x -20 °C freezers and 5 refrigerators and a cold room (walk-in chamber) maintained at -20 °C. Two freezers of -20 °C were kept outside the Deep freezer room. However, they were accessed by only the Deep freezer custodian. The temperature monitoring of one of the Deep freezer was tested.

The alarm connected to the security room was triggered in a timely manner and notification was sent to the custodians. The data logger for the period of the study in the scope of the inspection was provided and reviewed. Entrance and exit to the Deep freezer room was provided by key-card and was not logged in the logbook.

SOP for operation, calibration, performance verification and maintenance of liquid handling devices effective 26 Oct 2017 version 6 was used and the calibration of micropipette was demonstrated. The validated Excel sheet was used for calculation purposes. The SOP was not sufficiently clear to ensure that ten consecutive measurements of the volume of liquid (water) would be made. The SOP could be improved by clarifying the number of required measurements.

The external calibration of the microbalances covered the repeatability, eccentricity, linearity, sensitivity and minimum weight tests and hence considered complete. The calibration certificate for selected equipment was reviewed.

An emergency shower and eye-wash station were tested regularly. An emergency aid-kit was available. The MSDS binder was indexed and after discussion with inspection-team, arranged alphabetically.
A List of equipment and instruments used in the studies was provided.

The inventory log book for the equipment at Insignia was provided.

The Report on the temperature mapping of deep Freezer performed on 21-23 May 2016 by the service provider was reviewed.

At the back of each freezer logbook for record of storage and retrieval, there were also pages for recording respective instrument failure(s). Any repair could be linked to a template for service report which was issued by QA and the accountability and request record was kept, with reference to the finding.

The reagents were procured from the commercial sources. The chemicals were labelled appropriately, e.g. received by, storage condition, use before date, opened date, opened by, use before date after opening. Solutions prepared were also labelled appropriately, including the purpose for the preparation (i.e. either for MD/MV/Study ID), solution name, prepared by, prepared on date, batch no. of the solution, use before date, storage information etc.

The Disposal of waste was carried out according to the instruction fixed to the wall.

The weighing room was separated from the rest of facility. The internal and external calibration of the balances was performed adequately.

The observations made related to this section were adequately addressed in the CAPA provided by the CRO.

Pharmacokinetic, statistical calculations and reporting section

21. Pharmacokinetic, statistical calculations

The Pharmacokinetics and Biostatistics Department was located at Shivalik B-wing & Vedant.

The Randomization schedule was generated on request from the Clinical department by email. The process of request of randomization list according to the applicable protocol was adequate.

The pharmacokinetic and statistical department consisted of seven statisticians, led by the group-lead qualified for the designated tasks. The process of statistical and pharmacokinetic calculation was explained in detail by the group – Lead.
Calculations were made using SAS and Phoenix WinNonlin software systems, both server-based and with access restricted to only the statisticians. The IQ for SAS was performed on the server on which SAS software was installed. A log file was generated in the SAS software to record the history of the activities.

The history of the calculation was captured by the WinNonlin study by study. Data values input was double checked by the QA-team.

Bioanalytical results were locked in the software system in accordance with the applicable procedure. Only the database manager and operator were authorised to unlock the data and the activity would be captured by the audit trail.

Clinical results were captured only on paper and archived in the archiving facility according to the applicable procedures. The Excel sheet containing the time deviations and other relevant data was sent to the PB by email, after approval by the QA department.

The observations made related to the pharmacokinetic were adequately addressed in the CAPA provided by the CRO.

### 22. Study report

The final report was compiled in accordance with the ICH E3 guideline or applicable regulatory requirement. All details as required were compiled by the report writers from respective departments.

The results/concentrations of individual subjects obtained during a project sample analysis with details of calibration curve standards and quality control samples including the discussion about the methodology adopted, and other requisite details were compiled in a bioanalytical report as per applicable regulatory requirement.

<table>
<thead>
<tr>
<th>Miscellaneous</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Samples taken</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Assessment of the CRO master file</strong></td>
<td>CRO MF was available.</td>
</tr>
<tr>
<td><strong>Annexes attached</strong></td>
<td>Not applicable</td>
</tr>
</tbody>
</table>
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 and GLP at *Veeda Clinical Research*; located at following sites:

- *Shivalik Clinical, Pharmacokinetics & Bioanalytical Facility; Shivalik Plaza A, Near IIM, Ambawadi, Ahmedabad, 380 015; India*

- *Vedant Clinical, Pharmacokinetics & Bioanalytical Facility; 2nd, 3rd & 4th Floor, Vedant Complex, Nr. Y.M.C.A. Club, S.G. Highway, Vejalpur, Ahmedabad, Gujarat, 380 051; India*

- *Insignia Bioanalytical Facility; Rev. Sur. No. 12/1, Insignia, Corporate House, Nr. Grand Bhagvati Hotel, Sindhu Bhavan Road, S.G. Highway, Bodakdev, Ahmedabad, Gujarat, 380054; India*

- *Skylar Screening Facility; 601 to 608, 6th Floor, Skylar. Corporate Road. Prahladnagar, Ahmedabad-380015, Gujarat; 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.
<table>
<thead>
<tr>
<th>Part 4</th>
<th>List of guidelines referenced in the inspection report</th>
</tr>
</thead>
</table>
   **Short name:** WHO BE guidance  
   **Short name:** WHO multisource guidance  
   **Short name:** WHO GCP  
   **Short name:** WHO TRS No. 996, Annex 5 WHO GDRMP guidance  
   **Short name:** WHO GLP  
   [http://www.ispe.org/gamp-5](http://www.ispe.org/gamp-5) |
8. WHO Operational guidelines for Ethics Committees that review biomedical research (7). WHO, TDR/PRD/ETHICS/2000.1
   http://www.who.int/entity/tdr/publications/documents/ethics.pdf?ua=1


    http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=11&showFR=1

11. EU guidelines to Good Manufacturing Practice and Medicinal Products for Human and Veterinary Use Annex 11, Computerized systems

    **Short name: WHO TRS No. 961, Annex 9**

    **Short name: WHO TRS No. 957, Annex 7**

14. Glove use information leaflet, Patient Safety, save lives clean your hands, WHO, revised August 2009
    http://www.who.int/gpsc/5may/Glove_Use_Information_Leaflet.pdf

15. WHO Good Clinical Laboratory Practices (GCLP)