### Part 1 General information

#### Organization details

<table>
<thead>
<tr>
<th>Company information</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Name and Address of the Site inspected (Clinical site)</strong></td>
<td>Sun Pharmaceutical Industries Limited Hakeem Abdul Hameed Centenary Hospital (2nd Floor) Jamia Hamdard University, Hamdard Nagar New Delhi 110062 India</td>
</tr>
<tr>
<td><strong>Corporate address of Organization</strong></td>
<td>Sun Pharmaceutical Industries Limited SUN HOUSE, CTS No. 201 B/ I, Western Express Highway, Goregaon (E) Mumbai 400063 India</td>
</tr>
<tr>
<td><strong>GPS coordinates</strong></td>
<td>Latitude 28.5151 Longitude 77,2510</td>
</tr>
<tr>
<td><strong>WHO product numbers covered by the inspection/ Product names/ Study numbers/ Study titles</strong></td>
<td><strong>Study no. DLG_50T_0600_17</strong> Single dose two-way crossover bioequivalence study on Dolutegravir tablets 50 mg in healthy adult human subjects under fasting condition. <strong>Study no. DLT_50+300+300T_0415_17</strong> Single dose two-way crossover bioequivalence study of Dolutegravir, Lamivudine and Tenofovir Disoproxil Fumarate tablets 50mg/300mg/300mg in healthy adult human subjects under fasting condition.</td>
</tr>
</tbody>
</table>

#### Inspection details

| Dates of inspection | 10-11 January 2019 |
| Type of inspection | Routine |

#### Introduction

The site had an aim to provide clinical pharmacokinetic studies in healthy human volunteers for approval of drug candidate for marketing in domestic and international markets. The source of formulated drug candidate was the formulation and development unit of SPIL or any other manufacturer.
of finished product under cGMP conditions. The aim of the Clinical Research facilities was to assess the bioavailability and conclude bioequivalence between the test drug and a similar Reference Listed Drug from innovator or the equivalent form of any other manufacturer. The centers also carried out bioavailability studies of newly formulated drug candidate to study the pharmacokinetic parameters of the drug candidate.

<p>| General information about the company and site | Sun Pharmaceutical Industries Limited established in 1983 and headquartered in Mumbai, India, is an international, integrated pharmaceutical company, with 45 global manufacturing facilities. Sun Pharma acquired Ranbaxy in March 2015. Approximately 2000 products were produced by the company around the world and the company was ranked as number one in India with regard to the number of products produced. In addition to manufacturing and bioanalytical sites, the company, in India consisted of three CPU units located in New Delhi and Vadodara. The clinical site in New Delhi as a part of Gurgaon facility was leased from Hakeem Abdul Hameed Centenary Hospital and was located on the second floor of the hospital. |
| History | The Cooperate was inspected by various regulatory authorities, including USFDA, MHRA, ANVISA, ANSM, Malaysian MOH, MCC, GCC and CDSCO. Last inspection by WHO was conducted in 2013 in Hamdard Nagar. |
| Brief report of inspection activities undertaken | The scope of the inspection included a review of the following study-related activities: 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. |
| Scope and limitations | Out of scope This site was a clinical site only. |</p>
<table>
<thead>
<tr>
<th>Abbreviations</th>
<th>Definition</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>
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<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>HPLC-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>
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<tr>
<td>IQ</td>
<td>installation qualification</td>
</tr>
<tr>
<td>LIMS</td>
<td>laboratory information management system</td>
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<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>
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<tr>
<td>PQ</td>
<td>performance qualification</td>
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<tr>
<td>PQS</td>
<td>pharmaceutical quality system</td>
</tr>
<tr>
<td>QA</td>
<td>quality assurance</td>
</tr>
</tbody>
</table>

Abbreviations

Legend:

- **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
- **CTM**: clinical trial manager
- **CoA**: certificate of analysis
- **CSR**: clinical study report
- **DQ**: design qualification
- **ECG**: electrocardiogram
- **GAMP**: good automated manufacturing practice
- **GCP**: good clinical practice
- **GLP**: good laboratory practice
- **GMP**: good manufacturing practice
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- **IB**: investigator’s brochure
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- **IQ**: installation qualification
- **LIMS**: laboratory information management system
- **LLOQ**: lowest limit of quantification
- **LOD**: limit of detection
- **MS**: mass spectrophotometer
- **MVR**: monitoring visit report
- **NRA**: national regulatory agency
- **OQ**: operational qualification
- **PIS**: patient information sheet
- **PQ**: performance qualification
- **PQS**: pharmaceutical quality system
- **QA**: quality assurance

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Contact: prequalinspection@who.int

Sun Pharma Industries Limited, Hakeem Abdul Hameed Centenary Hospital: New Delhi, India -BE

10-11 Jan 2019
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.

The following clinical Pharmacology units located in India were organized and managed by Sun Pharma Industries to conduct clinical studies of products produced by the company:

- Clinical Pharmacology Unit at Hakeem Abdul Hameed Centenary Hospital
  2nd floor, Jamia Hamdard University
  Hamdard Nagar
  New Delhi
  110062, India

- Clinical Pharmacology Unit Sun Pharmaceutical Industries Ltd
  Tandalja, Vadodara Gujarat
  390 012, India

- CPU Akota, Vadodara with a total capacity of 148 beds, divided in four clinical wards. However, this site was not in the scope of this inspection as none of the clinical activities related to the WHO-applications were performed at this site.

The Organizational chart depicting key positions and the names of responsible persons was available. Additional organograms for R&D/PV Quality, Gurugram GCP QA, and for clinical laboratory were presented.

The general working hours were from 8:30am to 5:00pm. However, additional shifts were required during admission of volunteers.
2. **Computerized systems**

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

   The access control was handled by IT using a “User access Management form” completed by responsible department, upon the employment of staff.

   An evaluation was made by the system- and technical-owner to define the procedure for backup and restoration by completing the “Backup selection request” form with necessary approvals. A backup policy and schedule were then created. Four types of backups were arranged: daily (incremental), weekly, monthly and yearly.

   Restoration of media regularly took place to ensure that the data collected on the tapes remained fully readable. The tape could not be browsed in case the media was corrupted. In that context, all files were browsed to ensure that no file was corrupted.

   A computerized system inventory was provided with record of validation status, last validation date and review frequency as well as next review. The review frequency was established based on a risk assessment category system implemented in SOP for Computerized systems periodic validation review.

   The server used for PMS data-system was located in Gurgaon. The qualification documentation for PMS data-system was reviewed. The system was in use since June 2012 followed by a revision on 12 Oct 2017. The revision history was also available, with a full description of each change, linked to an ID number, which was adequately defined.

   SOP for computerized system validation was reviewed.

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. The independency of QA unit was ensured by using autonomous reporting route throughout the organization.

   An adequate CRO Master File, version 05, including CPU’s layout, flow chart, list of major equipment, list of validated software, organizational structure, key personnel CV and JD, list of SOPs and list of service providers was provided.

   A Global Quality Manual document which applied to the Clinical Research operations at Sun Pharma's Research and Development (R&D) including Bioavailability and Bioequivalence (BA/BE) Studies and Clinical Trials was available. This manual was globally applicable to the Clinical Research operations at Sun Pharma's R&Ds and included all the GCP Quality System Elements of the Quality Management Systems (QMS).
The company’s QMS consisted of:

- Quality policy
- Quality manual
- Global standard operating procedures
- Site specific standard operating procedures
- Forms – templates / Logbooks

SOP, GQS (Global Quality System) and Study Protocol Management were managed by DCM database. In case of any required revision of SOPs, a change control would be raised in the DCM. SOP for Change control; was reviewed. The SOP was applicable to any changes in the organization with adequate description. Updates on requirements were also addressed and implemented in their system.

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:

- performing study specific audits
- performing internal system audits
- performing audits of service providers
- review of SOPs
- review of study protocols
- issuance of raw data forms-study specific according to SOP OP005639 for recording, reviewing and management of raw data

Furthermore, each unit had their own QC team to report to the management of the site.

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

Planning, conducting and reporting of internal system audits was performed in accordance with the applicable SOP. Annual system audit schedules for 2018 and 2019 were provided. The audit report pertaining to the audit performed in December 2018 was reviewed to verify the independency of the auditors. A comprehensive CAPA plan was provided by the respective unit.

The QC unit was independent and directly reported to CPP-Head, Dr Arshad.

The translation company used at the site was audited by the company on 13 Apr 2018. The CAPA was provided and adequately assessed.

Review of the contracts was executed by the legal entity using the DMS.
4. Archive facilities

The archive facility was located on the 2nd floor with the rest of the facility and managed by archivist. The SOP for archival, retrieval & disposal of the documents at CPU, New Delhi was reviewed.

The archive 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. The pest control contract with PCES was available.

Folders were correctly arranged based on the type of documentation. At the New Delhi site, only logbooks, and personnel documentation such as training records were kept.

The retrieval of 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; Archive Facility Recall India Information Management dated 28 Aug 2014 was available. The original contract was signed by Ranbaxy representative; however, the contract was renewed by Sun Pharma which was valid from Sep 2016.

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 the 2nd floor of Majeedia Hospital, Jamia Hamdard Nagar, New Delhi, since 1994. The lease agreement with Jamia Hamdard Universtiy was available, signed on 1 Aug 2009. The agreement was renewed with Sun Pharma on 11 Apr 2016.

The premises consisted of:
- Volunteer reception area
- Changing room with lockers
- ICF presentation area and obtaining area
- Screening area, including enrolment, screening, HIV counselling, sample collection and medical examination and ECG
- Phlebotomy, which was temperature controlled
- Sample separation area, with refrigerated centrifuges, deep freezers
- 6 CPU wards with 14 beds at each ward
- Toilets and showers
- 3 bedded – ICU
- Pharmacy
- Dining area
- Archive facility

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. The facilities were accessed by a key-card issued by Admin-department. 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. There was a 380 kVA Diesel Generator (DG) set for power generation with the respective SOP and maintenance logbook available. Additionally, 2 UPS for 16 kw each total of 32 kw were in use at the site.

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

The facility used for disposal of waste was visited to ensure that related environment-friendly measures were established. The service agreement for bio-medical waste disposal was dated 1 Aug 2016 with Biotic waste solutions Pvt. Ltd. Chemicals waste from clinical laboratory was separated and led to the ETP (Effluent Treatment Plan) structured for the entire hospital.

The Eurotherm temperature recording system was used for 24-hour digital temperature monitoring device/recorder. Temperature monitoring of pharmacy for the period of dispensing of the study in the scope of inspection was reviewed.

The ECG machine used at the site had a storage option with respective audit trail. The results were communicated through CLIS data-system. Only admin had the right to modify the privileges in the software. Log-in activities were captured in the audit trail and the reason for the activity was documented in a logbook. The ECG results for three studies were compared.

**ICU**

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 appropriately carried out.
Pharmacy
The Pharmacy area was designed to store and dispense the Investigational Products. The Pharmacy area was well organized, access-controlled by key card and equipped with Pharmaceutical refrigerator, racks for storage of IMPs and laminar air flow bench. IMPs were arranged by projects. Retained IMPs were kept separately, and they were adequately labelled.

Calibration certificate of the HEPA filter of the LAF hood was provided by Belz Calibration Lab on 24 Aug 2018; providing the following test:

- Particle count test
- Integrity test result (using aerosol photometer)
- Velocity

The observations made with relation to the premises were 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. 30 employees on permanent contract and 48 on temporary contract were involved in site’s different activities at the time of inspection.

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

A period-specific delegation list of the authorized personnel performing tasks during each study was kept with the study binder, with their initials for identification purposes. Protocol training was a self-training procedure which was documented on the delegation list. The delegation list for study DLG_50T_0600_17 was reviewed.

The SOP for Responsibilities of clinical study coordinator was reviewed. The SOP was applicable for the period of the study no. DLG_50T_0600_17.

SOP for Training of personnel was reviewed. A training curriculum was developed based on the responsibilities and functions for a position / job role, categorized in three groups:

- Onboarding training
- Department training
- Job specific training
All the training curriculums of the departments constituted Master Training Needs Matrix. Applicable SOPs and requirements were listed on the matrix, and trainings were arranged by categories and subcategories. The training matrix was also implemented in their electronic learning system (e-LMS). Trainees should be registered within the system for curriculum of training activity, followed by online assessment (where applicable) and completion of e-signature. SOPs were effective as soon as 80% of the applicable staff had completed the training. The remaining staff would be tracked and followed up to ensure that the training was completed. Untrained staff were not allowed to participate in the respective activity.

**Clinical section**

7. **Clinical phase**

The facility was clean, well ordered, easily accessible and appropriate for the intended number of study subjects. Certificates of calibration of selected instruments were reviewed. Generally, equipment used in clinical sites were calibrated by external service providers at pre-defined intervals and labelled properly. However, the fingerprint scanner was not working accurately, and a proper calibration was not carried out.

The site consisted of six CPU wards with sufficient space for 84 + 3 special care beds to accommodate the study subjects. The CPUs allowed supervision by the custodians during check-in periods. 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 emergency alarms at each bed which were randomly tested both in the CPU and in the showers. At the time of visit, the beds were not suitably arranged to give the subjects immediate access to the emergency alarms. Clothing kits were placed in the changing room and lockers for storage of subjects’ personal items were provided.

A memorandum of understanding for using Majeedia Hospital for Emergency medical services and X-ray was available. The initiation of studies was not communicated with the hospital prior to each study. However, the site was located at the 2nd floor of the hospital. A Mock Drill Exercise on management of medical Emergencies was performed on 31 Oct 2018 to establish the timely access to the emergency room.

Sample size estimation was given in the study protocol section 9.1 which was estimated based on available in-house data on substances. T/R ratio was assumed to be in the range of 90-110%, and Intra-subject CV was estimated approx. 25%. Hence, 56 subjects were assumed to yield a power of 80% to show BE. Additionally, the study design took the risk of drop outs and withdrawals into consideration and recruited 66 subjects overall for one of the studies in the scope of inspection.
8. Clinical laboratory
The facility’s clinical laboratory was accredited by:
- CAP (College of American Pathologists)-USA, until 11 Jan 2020
- NABL (National Accreditation Board for Testing and Calibration Laboratories)

The laboratory was responsible for hematology, biochemistry, serology, immunohematology and urine examinations and had undergone proficiency testing programs arranged by BIORAD-EQAS, ISHTM-AIIMS, CAP-USA.

SOP for Reporting of test results was provided. The lists of critical values and reference intervals biochemistry were provided and implemented in their practice, based on literatures given in the SOP.

The laboratory instruments were interfaced with CLIS application for bidirectional communication through barcodes affixed to the samples by the time of collection.

9. Ethics
Study DLG_50T_0600_17 protocol, ICF and other required documentation was approved by Jamia Hamdard IEC on 29 Dec 2017. A list of members was available, dated 16 Dec 2016.

Since the Ethics Committee belonged to the Majeedia Hospital, the conflict of the interest of IEC members was investigated by the review of the respective declaration of conflict of interest agreement, confidentiality agreement and training records. 14 protocols were submitted for approval on Dec 2017. One of the co-investigators was involved in one of the studies, however her conflict of interest was declared, and she was exempted from voting process.

Insurance certificate from ICICI Lombard General Insurance Company Ltd from 01 Jul 2017 till 30 June 2018 was provided.

10. Monitoring
Monitoring report for study no. DLT_50+300+300t_0415_17 was reviewed. The monitors were appointed by Sun Pharma. A total of 9 visits were performed by two monitors and documented in the visitor logbook. Monitors’ CVs were available.

11. Investigators
The randomly selected investigators’ CV, training log and medical license were reviewed.
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 logbooks and PMS.

Tests and reference products were received at the CPP facility (Bioanalytical site). The details of the products such as certificate of analysis, airway bill, and regulatory approval letters were scanned and kept in the PMS database.

Upon the receipt of samples at the clinical site’s pharmacy, number of containers and shipment condition were verified, and all required information was recorded in the PMS in accordance with the SOP for receipt, retention, archiving, retrieval and transfer of investigational products.

Records for the shipment, the respective datalogger ID number, delivery, COA, receipt, description, storage (including storage condition), dispensing, reconciliation, return and retain of any remaining pharmaceutical products were verified for study DLG_50T_0600_17.

Dispensing of the IMPs was adequately carried out in accordance with SOP for dispensing of IPs. The labelling was performed in accordance with the requirements and the administration of dosing was directly recorded in the CRF. The tear-off portion of labels was pasted onto the CRF.

13. Case report forms

Screening reports of randomly selected subjects participating in study DLG_50T_0600_17 and study DLT_50+300+300t_0415_17, including time deviations for IP administration and Blood sample collection were verified.

14. Volunteers, recruitment methods

The organization maintained a database of volunteers using CLIS database, from which suitable volunteers for studies based on the requirements of the study, were selected. Volunteers were informed by either word of mouth or phone calls 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 CLIS. Any changes to demographic data should be approved by designated personnel.
Volunteers were informed of the objective and procedures of the study and consent was obtained for their respective screening. 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.

Master List of subjects in study DLG_50T_0600_17 was verified to be aligned with the check-in day records, i.e. 9 Jan 2018 documented in the visitor logbook.

The OVIS (Online Volunteer Information System) database was linked with several other bioequivalence centres to avoid cross participation by subjects. Volunteers were blocked in the OVIS system prior to the first dose administration in the clinical site according to the list of admission. Blocking would be approved as soon as dose-administration was confirmed.

The Chest X-ray screening activities were performed at the hospital’s X-ray facility. The volunteers were sent to the facility after completion of other screening activities, if necessary.

Healthy Volunteers whose medical screening were assessed in CLIS (i.e. potentially eligible study subjects) were contacted & asked to report to the CPU on study initiation day (admission day of period 1). Volunteers reported to the CPU Reception for Study Admission. Volunteers’ personal information (incl. name, date & time of entry) were recorded at the entrance by the security personnel in a register logbook and an Entry Gate Pass was made for the respective volunteer. Pre-test counselling and post-test counselling HIV were done in accordance with the applicable procedure.

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 Form. Consent for the study was taken by the Investigator on a one to one basis and ICF obtaining was recorded. The volunteers were then admitted for housing to undergo the study procedure. The randomly selected ICFs were reviewed to confirm the signature of PI. At the time of studies in the scope of inspection, the face to face meeting with the subject was only performed by PI.

The results of subject screening activities were adequately recorded in the 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 with relation to this section were adequately addressed in the CAPA provided by the CRO.

15. **Food and fluids**
   
   Catering service was outsourced.

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

   The reconciliation of issued forms used for reporting of AEs and follow up of AE occurred in study DLG_50T_0600_17 was reviewed.

   AEs pertaining to the studies were verified in the CRFs for selected subjects.

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

   The sample collection did not take place during the inspection. However, it was verified that specification of plasma samples, sampling method, volume and number of samples were documented per SOP Preparation and storage of biological 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 and were stored in -25 and -78 °C 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. Four refrigerated centrifuges were used for study DLG_50T_0600_17. The usage of instruments was documented in the respective logbooks. The usage of instrument was verified for the period of the study. Haemolysis of the samples was identified and classified against the applicable chart and properly recorded in the respective study specific form. Aliquots were distinguished by label colour.

19. **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 Sun Pharma. The associated Forms, Formats and Log Formats, as well as data-systems mentioned in section 2 were also developed to capture the information/data that was required to be documented.
Study Protocols, Study plans, Informed Consent Documents, Case Report Forms, and other documents that provided guidance in conduct of clinical 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.

The unused logbooks were returned to the QC for further processing.

SOP for Recording, reviewing and management of raw data was reviewed. Request for issuance of forms was sent to the QC, followed by the steps detailed in the SOP to issue the forms and keep the accountability. The issuance history of adverse events form used to report and follow up of AEs was reviewed to verify the issuance of the templates and forms.

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

22. Study report

Study reports were provided and used during the inspection to ensure the compliance.

<table>
<thead>
<tr>
<th>Miscellaneous</th>
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<tbody>
<tr>
<td>Samples taken</td>
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<tr>
<td>Assessment of the CRO master file</td>
</tr>
<tr>
<td>Annexes attached</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 Sun Pharmaceutical Industries Limited located at Hakeem Abdul Hameed Centenary Hospital; (2nd Floor) Jamia Hamdard University, Hamdard Nagar, New Delhi 110062, 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

   **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

   Guidance, Pharmaceutical Inspection Convention Pharmaceutical Inspection Co-operation

    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

12. Model guidance for the storage and transport of time-and temperature-sensitive
    pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical
    Short name: WHO TRS No. 961, Annex 9

13. Guidelines for the preparation of a contract research organization master file, WHO
    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)