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| **TGHN-256x151px**  **Standard Operating Procedure** | | | **SOP No:**  **Version: 1**  **Effective Date:** | |
| **Title:**  **Site Initiation, Activation, Conduct and Close-out** | | | | |
|  | NAME | **SIGNATURE** | | **DATE** |
| **PREPARED BY** |  |  | |  |
| **REVIEWED BY** |  |  | |  |
| **QA UNIT**  **AUTHORITY** |  |  | |  |
| **APPROVAL**  **AUTHORITY** |  |  | |  |

**7.1 Purpose**

To describe the process which ensures that the site is organized and prepared for the proper conduct of the research study at [INSTITUTION]. This standard operating procedure (SOP) also describes the processes to be followed at site initiation, activation, conduct and closeout of research study at [INSTITUTION].

**7.2 Scope**

This SOP will apply to all pharma sponsored research study initiation, activation, conduct and close-out at [INSTITUTION].

**7.3 Procedure**

A research study should be initiated at a site only after investigator and Sponsor/CRO involved in the study is satisfied that essential documents, agreements and approvals are all in place. The site initiation process is designed to ensure that;

* The site has all essential documents in place for the site to conduct the study in compliance with the approved protocol and applicable regulatory guidelines.
* The site is aware of all the sponsor’s procedures and SOPs for study conduct (such as safety recording and reporting, amendments, notification of any urgent safety measures/ violations or serious breaches) and has read and understood each.
* The site is met with all the required regulatory and sponsor requirements.

**7.3.1 Preparing site for Site Initiation Visit**

a. For preparing the site for initiation the investigator(s) or Clinical Trial Coordinator (CTC) should:

* Confirm the available date and time with the clinical research team that must attend the meeting and arrange the most suitable meeting date, time and place.
* Request an agenda for the visit from the sponsor; circulate the same to each team member.
* Confirm that investigator and team has reviewed the Protocol and Investigator’s Brochure (IB) and any up-to-date information on investigational product (IP). The Investigator(s) must prepare a list of questions if any to be asked in the SIV.
* Ensure that the procedures stated in the study protocol are applicable at the site and fully understood.
* Confirm that all documents required by Institutional Ethics Committee (IEC) are available.
* Confirm that the clinical trial agreement (CTA), indemnification letter and budget are finalized and signed.
* Notify appropriate departments regarding the sponsor/CRO visit (e.g., Laboratories, pharmacy, CT scan, bone scan and x-ray, etc).
* File all essential documents in TMF (or sponsor-supplied Investigator Study File), and compile any outstanding documents to provide to the Clinical Research Associate (CRA) at the initiation meeting.

**7.3.2 During the Site Initiation Visit**

a. During the initiation visit the investigator(s) or Clinical Trial Coordinator (CTC) should:

* Ensure that the Investigator’s Trial Master File (TMF) contains the following mentioned applicable items and all the required regulatory documents:
* Signed protocol and Investigator Statement o Signed and executed Investigator contract CVs and licenses of key site study staff
* Financial Disclosure forms
* Investigator Undertaking (IU)
* Form FDA 1572 for IND studies
* IEC approval letter for the protocol o IEC membership roster (updated)
* IEC approved informed consent form
* Institutional and/or other regulatory authority approvals or Valid clinical/other laboratory licensure
* Laboratory normal value ranges
* Notice that indicates the study has been submitted to the regulatory authorities (if applicable).
* Investigator Brochure, if applicable
* Case Report Forms (CRF)
* Investigational product inventory management forms or any other essential documents.
* Provide the study members name involved in the study and their responsibilities in the duty delegation to the monitor/CRA.
* Provide original and updated curriculum vitae of all study personnel / Investigators involved, as per sponsor requirements (if not provided earlier).
* Ensure that the names and contact numbers of the relevant medical and study personnel of the sponsor are available and documented clearly.
* Ensure that all relevant study site personnel fill out the Site Personnel/Signature Log and Training Log.
* Check that the procedures and plans for storage, dispensing and return of IP have been agreed and finalized with the Sponsor and Pharmacist (if applicable).
* In case of paper CRF’s: Check that the quantity of CRFs that have been requested or shipped to the study site are sufficient for the number of Participants/patients that are likely to be recruited into the study also allowing for the archiving of one set of intact, unused CRFs
* Check that other related supplies are available or are to be shipped to the study site at a later date, and that they are available in sufficient quantities.
* Check that laboratory facilities and arrangements for the dispatch of samples to the central laboratory are organized and that any specialized equipment that may be required will be available throughout the period of the trial, e.g. collection kits, centrifuge machine, freezer, etc.
* Ensure that monitor/CRA gives sufficient time to CTC for CRF completion training.
* Ensure and understand the requirements of the sponsors/CRO regarding source documents and raw data, which will be required during monitoring visits to enable the monitor/CRA to perform source data verification at each monitoring visit.
* Ensure that the procedures relating to the archiving of study records at the end of the study is agreeable to the sponsor.
* During the initiation visit the Investigator or delegate (for investigator initiated study) and monitor/CRA (for sponsor study) will provide a protocol-specific training session to all the members of the research team who will be involved in the research study. The investigator or monitor/CRA will ensure that the attendance sheets and other training documentation are completed.

b. The protocol-specific training session will include, but is not limited to, the following:

* Aim and Objective of the protocol
* Time and events schedule for the protocol
* Subject recruitment
* Obtaining informed consent
* Procedure for dispensing the IP
* IP storage and records
* Protocol-specific forms and procedures
* Source documentation
* Adverse event reporting
* Additional information from the Investigator’s Meeting (IM)
* Any other relevant information

c. The Investigator, monitor/CRA and CTC will:

* Develop a recruitment plan for subjects
* Identify a back-up to the primary CTC

**7.3.3 Study Activation and Initiation Visit Follow-Up**

In preparation for study activation:

* Confirm that the sponsor sends a written summary of key discussions and agreements made during the site initiation visit. Follow-up if necessary.
* Confirm readiness of the site to start the study.
* Confirm the receipt of all study-related materials such as CRFs, laboratory supplies, investigational product(s).
* Distribute protocol summaries and worksheets, if not done previously (the sponsor may provide study-related worksheets, however the site can prepare one).
* Notify all appropriate departments that the study is ready to enroll participants.
* Initiate study recruitment strategies and begin enrolling study patients/participants.

**7.3.4 Study conduct**

a. Once the site is activated and starts recruiting patients, the Investigator and CTC will ensure the following:

* All study activities are accomplished according to the protocol and applicable regulatory regulations.
* Subjects sign the correct version of the consent form before any study-related procedures are accomplished.
* Data collected in the Case Report Form (CRF) are supported by source documents.
* Protocol deviations/non compliance/violations/waivers if any should be notified to the IEC (Refer SOP for IEC communication) and the same must be documented in the source documents and appropriate CRF.
* Adverse events are reflected in the source documents and captured in the CRF. (With appropriate term, grade, causality, start and stop date and CCM given if any.)
* Serious Adverse events (SAEs) are reported to the Sponsor/CRO and IEC within specified time frame (refer SOP for SAE reporting).
* SUSAR and CIOMS should be notified in the timely manner to the IEC.
* The IP is being dispensed correctly and IP accountability records are being maintained.

b. While the study is ongoing, the CTC will ensure the following

* The Sponsor/CRO is informed of all significant study events and staff members are documenting critical interactions with the Sponsor/CRO.
* Biological samples are being obtained, handled, stored, and shipped appropriately.
* Study supplies remain adequate. Study records remain confidential.
* All equipment is calibrated regularly and maintenance records are being kept.

**7.3.5 Premature Termination or Suspension of a Study**

a. If the research study is prematurely terminated or suspended for any reason, the investigator/institution should:

* Immediately inform the IEC regarding the premature termination of the study in the format specified in the IEC SOP.
* Promptly inform the trial participants and include, where appropriate, the reason for suspension / early termination of the study.
* Assure appropriate therapy and follow-up for the participants, and, where required by the applicable regulatory requirement(s), should inform the regulatory authority (ies).
* The PI should maintain documents as specified in the TMF list and take measures to prevent accidental or premature destruction

In addition:

b. If the PI terminates or suspends a research study without prior agreement of the sponsor, the PI should:

* Promptly inform the sponsor and the IEC regarding the termination Provide the sponsor and the IEC with a detailed written explanation of the termination or suspension.

c. If the sponsor terminates or suspends a research study, the PI should:

* In case the sponsor chooses to or is required to terminate prematurely or suspend the research study, then the sponsor should notify the investigator(s), institution(s), the ethics committee and the regulatory authorities accordingly. The notification should document the reason(s) for the termination or suspension by the sponsor or by the investigator / institution

**7.3.6 Site close-out**

a. Preparing the site for study close-out visits:

* After the last patient has completed all scheduled visits associated with the study, arrange a mutually convenient date and time with the monitor/CRA to conduct the study close-out visit.
* Request the monitor/CRA for the visit agenda so key research personnel such as PI, Co I, CTC, research nurse and other team members will be available, as appropriate.
* Ensure all regulatory documentation and case report forms (CRFs) not previously monitored are complete and available for review.
* Ensure all data queries received to date have been resolved.
* Inventory IPs supply and complete final accountability records. If previously instructed to return or destroy IP, assure all required documentation is filed in the appropriate TMF for monitor/CRA review.
* Arrange monitor/CRA meeting with the PI and/or Co I and CTC to discuss any outstanding issues.
* PI will ensure that all outstanding payments are cleared as per CTA.

b. Managing the study close-out visit:

* Ensure all documentation (e.g., regulatory correspondence) is filed appropriately and ready for the monitor/CRA to review during the close-out visit.
* Discuss all open study-related issues and what steps will be taken to resolve them in order to satisfy the sponsor/CRO requirement(s).
* Review with the monitor/CRA the list of outstanding issues related to regulatory documents, source data verification, IP reconciliation, and any requirements for data retention and storage.
* Discuss any concerns regarding the possibility of a quality assurance audit and/or inspection by IEC or external regulatory bodies. Include the CTC as appropriate.
* If the study involved electronic data capture, determine when hard copies/CD of all CRFs will be provided to [Institution], if applicable.
* The PI is responsible for ensuring the appropriate follow-up, per the protocol, for any participant experiencing an ongoing unanticipated problem (e.g., serious adverse event) at study end and providing this information to the sponsor/CRO, assuring all requirements have been met.
* Arrange meeting of the PI and monitor/CRA to discuss any future considerations (e.g., publication of study data or future studies).

c. Follow-up after the study close-out visit

* For any remaining IP(s), ensure the item(s) is returned to the sponsor/CRO per their requirements.
* If the randomization code for any IP was broken for any reason, ensure complete documentation has been filed.
* Ensure return or destruction of all other study-related materials, such as unused lab kits and CRFs.
* Ensure any equipment on loan from the sponsor is returned or if mutually agreed by both the parties can be retained at the site.
* After all data queries have been resolved, check TMF, subject files and other study files for completeness.
* Arrange for transfer of study documents to secure storage.
* Submit the Final Closure Report to the IEC, in accordance with IEC SOP for Study Completion or Closure.
* Provide the sponsor/CRO with a copy of the IEC closure letter.
* Verify participant reimbursement or compensation if any have been distributed per the study budget, as outlined in the Informed Consent and CTA.
* If the informed consent and CTA, protocol or contract state subjects will be informed of their treatment arm, ascertain from the sponsor how and when this will be completed.

**7.4 Applicable Staff**

This SOP applies to all the personals of the clinical research team and others who may be responsible for site initiation, activation, conduct and close-out at [INSTITUTION].

These include the following:

* Investigator
* Research Team
* CTC
* Research Nurse
* Support staff

**7.5 Staff responsible for Implementation**

The PI and the research team will ensure that the research team involved in the conduct of the study will comply with this site SOP and research members involved in the study are following this SOP while communicating with sponsor/CRO.

The PI will ensure that at the time of implementation of the SOP, that the research team at the DEPARTMENT OF CLINICAL RESEARCH in [Institution] are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

Inform IEC that this site SOP will be implemented within the institution.

**References**

21 CFR 312.50 General responsibilities of sponsors

21 CFR 312.56 Review of ongoing investigations

21 CFR 312.59 Disposition of unused supply of investigational drug

21 CFR 312.60 General responsibilities of investigators

21 CFR 312.62 Investigator recordkeeping and record retention

21 CFR 312.64 Investigator reports

21 CFR 312.66 Assurance of IRB review

21 CFR 312.68 Inspection of investigator's records and reports

21 CFR 54.6 – Record Keeping and Record Retention

CDSCO guidelines: Appendix V

Good Clinical Practices

ICH Guidelines for Good Clinical Practice (E6)

May 1997 International Conference on Harmonization (ICH)

Schedule Y