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| **TGHN-256x151px**  **Standard Operating Procedure** | | | **SOP No:**  **Version: 1**  **Effective Date:** | |
| **Title: Interaction with Institutional Ethics Committee (IEC)** | | | | |
|  | NAME | **SIGNATURE** | | **DATE** |
| **PREPARED BY** |  |  | |  |
| **REVIEWED BY** |  |  | |  |
| **QA UNIT**  **AUTHORITY** |  |  | |  |
| **APPROVAL**  **AUTHORITY** |  |  | |  |

**4.1 Purpose**

To describe the procedures related to communication with the IEC during the entire study duration right from study initiation to completion, and to describe what documents should be retained to reflect interaction with the IEC.

**4.2 Scope**

This SOP will apply to all studies being conducted at [Institution].

**4.3 Procedure**

Interactions with the Institutional Ethics Committee (IEC) continue throughout the duration of a research study. Establishing effective ongoing IEC communication and reporting procedures are essential to the successful management of research studies. An effective working relationship with the IEC strengthens the team approach to the protection of participant safety in addition to enhancing compliance with applicable SOPs, guidelines and regulations governing research studies.

Interaction with IEC is required during the entire course of the research study.

**4.3.1 Initial Submission of project to IEC**

a. Detailed description of project submission

The PI/ CoI/CTC should submit all study related documents to the IEC, no fewer than fourteen (15) days before the scheduled meeting.

The PI/CoI/CTC should complete the IEC submission form (Refer IEC SOP) and PI must sign and date in the form wherever required. CTC will obtain the CoI and other member (e.g HOD, Manager DEPARTMENT OF CLINICAL RESEARCH) signatures.

PI/Co-I/CTC must check the submissions as per the IEC checklist (Refer IEC SOP) to ensure that all mandatory forms and documents are enclosed.

The CTC will submit the signed forms and documents to the IEC. These include but are not limited to:

* Covering letter with brief description regarding the list of documents enclosed for IEC approval, including the no. of copies submitted, document enclosed relevant version number and date of all the documents (AX1-V3/SOP 04/V3).
* Project submission Form as mentioned above
* Study protocol
* Other related documents necessary for initial review as mentioned in the IEC
* Curriculum Vitae and updated GCP certificate of the investigator and study team.
* IEC fees (i.e. INR 50,000) cheque in the favour of “AAAAAA Foundation”, in case of sponsored studies. IEC Annual fees (i.e. INR 40,000), Expidate Review & approval Fees (ie INR 10,000) and cheque in the favor of “AAAAAA Foundation” in case of sponsored studies.For inhouse studies IEC fees (i.e. INR 10,000) cheque in the favour of “AAAAAA Foundation”.IEC fess for approval of Protocols in a Satellite Site is INR 10,000 and annual fee of INR 10.000 cheque in the favour of “AAAAAA Foundation”.
* Number of copies required for IEC submission will be as per IEC SOP Note: One additional copy for PI Acknowledgement
* The PI/CTC should keep a copy of the acknowledged (IEC stamp with sign and date) submission letter of the above mentioned documents in the Trial Master File
* (TMF) and send scan or copy to the sponsor (via mail or courier as required by the sponsor).

b. EC Response

The PI and CTC should ensure that the letter of response from the IEC includes the following information:

* Clinical study identification, protocol number and title;
* Name and version date of all documents reviewed by the IEC.
* Date of review by the IEC
* Approval for the number of participants to be recruited in the study.
* Decision/opinion/approval of the clinical study, including required modifications, if any; (Note: Reply to the IEC in case of any suggested modifications)
* If conditional approval given, it is not valid for more than 6 months (Refer IEC SOP)
* Procedures for appealing the decision/opinion of the committee;
* Any other information, if applicable, as described in the IEC SOP
* Date of renewal of approval;
* Signature of the IEC member secretary and date of the response.
* Following Schedule Y and GCP (ICH 3.2.1 et 3.2.2) a list of the members of the Ethics Committee and their qualifications, as well as the procedures of the said committee should be available.

The PI/CTC should keep an original copy of the IECs approval letter in the TMF and provide one copy to the sponsor/CRO (via email/fax).

Immediately after receiving IEC approval, register the study on CTRI and if applicable on ClinicalTrials.gov

Notify IEC after receiving registration number.

**4.3.2 Study Progress**

PI can start project at site after receiving approval letter from IEC and as study progress at site PI must communicate with IEC for all required notification and reporting such as:

a. Major Amendments

* Notify the IEC of any changes to the protocol and/or informed consent and/or of new information on the investigational product no fewer than fifteen (15) days before the next scheduled meeting.
* All amendments should bear amendment number and version number with date(s).
* The CTC must make sure that all changes or modifications in the amended version are underlined or highlighted along with detailed summary of changes.
* The amendment /documents along with the covering letter should be accompanied by Amendment Reporting Form (Refer IEC SOP)
* Number of copies required for IEC submission will be as per IEC SOP Note: One additional copy for PI Acknowledgement
* The PI/CoI/CTC should obtain a copy of the acknowledged (IEC stamp with sign and date) amendment submission letter of the above mentioned documents, and file the same in relevant section of TMF and send Scan or a copy to sponsor/ CRO (via email/fax).
* The amendments in the protocol and/or informed consent and of new information on the IP will be valid only after IEC approval, and should immediately implement the documents at the site after approval.
* Document the approval letter in the relevant section of the TMF and send a copy to sponsor/CRO( via email/fax)

b. Minor amendments and notifications

Minor amendments are those that do not increase the risk or decrease the potential benefit to subjects and may be approved by the IEC (Refer IEC SOP).This may include but may not restrict to:

* Renewed insurance policy
* DCGI and DGFT approvals
* Administrative notes
* Documents of administrative nature

**4.3.2.2 Deviations/Violation and Waivers**

Submit protocol deviations/violations and waivers to the IEC for review and approval according to IEC and regulatory requirements

Deviation/ non-compliance/ violation/waiver happens at site, when investigators/ trial sites, fail to :

* follow the procedures written in the approved protocol
* comply with national / international guidelines for the conduct of human research
* fail to respond to the IEC requests
* PI/CoI//CTC must submit the deviations /violations/waiver reports as per the IEC SOP.

Protocol deviation/ non-compliance/ violation/waiver can be detected during monitoring visit for the investigator initiated study by IEC and for sponsored studies by the monitor/ CRA also. Sometimes it can be detected by PI /study team member.

The IEC members and/or monitor/ CRA performing monitoring of the project at study site can detect protocol deviation/non-compliance / violation, if the project:

* Is not conducted as per protocol / national / international regulations
* when scrutinizing annual / periodic reports / SAE reports
* failed to respond to requests from IEC within reasonable time limit
* failed to adhere to protocol required procedures

A Protocol Waiver is analogous to a Protocol Deviation, except that prior IEC approval must be obtained before implementing the necessary departures from the protocol. Therefore, Protocol Waivers are anticipatory, while Protocol Deviations are not. E.g. Protocol Waiver means a prospective decision by a sponsor or investigator to permit accrual of a subject who does not satisfy the approved inclusion /exclusion criteria for enrollment.

IEC action could include one or more of the following:

* IEC will inform the PI that IEC has noted the violation / noncompliance / deviation and inform the PI to ensure that deviations / noncompliance / violations do not occur in future and follow IEC recommendations.
* IEC will enlist measures that the PI would undertake to ensure that deviations / noncompliance /violations do not occur in future call for additional information
* Suspend the study till additional information is made available and is scrutinized o Suspend the study till recommendations made by the IEC are implemented by the PI and found to be satisfactory by the IEC Suspend the study for a fixed duration of time
* Inform the Medical Director, [Institution]
* Revoke approval of the current study
* Inform DCGI / Other relevant regulatory authorities
* Keep other research proposals from the PI/ Co-PI under abeyance o Review and / or inspect other studies undertaken by PI/Co-PI
* File the IEC acknowledged deviations/violations and waivers forms submitted in relevant file and send one copy to the sponsor/CRO.

**4.3.2.3 Safety Information**

Safety information can be any information recently reported or obtained from sponsor/CRO particularly regarding risks associated with the research.

Safety information is categorized as Serious Adverse event (SAEs) and unexpected event reports of both onsite and offsite.

The Principal Investigator must review safety information received from the sponsor. It is recommended that the PI review of safety information must be documented.

The Investigator must submit Serious Adverse Events (SAEs) and unexpected events reports, both onsite and offsite, including follow up reports for active study participants.

Report all safety information to the IEC according to the IEC and regulatory requirements (eg. Investigational New Drug [IND] submissions, Council for International Organizations of Medical Sciences [CIOMS] reports, Suspected Unexpected Serious Adverse Reaction (SUSAR), Periodic Safety Update Report (PSUR), Data Safety Monitoring Board [DSMB] reports).

File the safety reports and any associated IEC correspondence, if any, in the TMF.

Copies of the associated IEC correspondence should be provided to the sponsor according to sponsor requirements.

Report any other information to the IEC that may adversely affect the safety of the participants or the conduct of the research study.

a. Off Site Safety Reports

Off Site SAEs are adverse event reports that are serious, expected, unexpected, related and unrelated (definitely, probably and possibly) to the drug and need prompt reporting to the IEC

The SAEs that are expected (if listed in the informed consent and IB) or unexpected but unrelated to the drug (classified as per the Offsite SAE Classification form – as per IEC SOP) have to be logged by the PI and to be submitted timely. The following log will be maintained continuously until the end of the study.

IEC will accept the log of the SAEs every 3 months and/or at the time of continuing review/ annual status report.

Those off site SAEs which qualify for prompt reporting, (classified as per the Offsite SAE Classification form – as per IEC SOP) will be reported to IEC secretary.

The Sponsor/CRO will send two sets of the offsite SAE, CTC will submit one to the IEC (as per the IEC SOP) and file acknowledged (Stamped, signed and dated by the IEC /DSMSC) copy in the TMF and send a copy to the sponsor/CRO.

PIs must review the SAE listings in detail and report if a trend is observed and communicate the same to IEC.

PI/Co-I may receive email or letter as applicable, if any queries are raised by the IEC Secretary. PI/Co I must reply to the query immediately.

b. Onsite SAE reporting:

Kindly Refer to SOP for Safety Reporting

4.3.2.4 Annual Report/ Continuing Review report

The purpose of Annual report/ continuing review report is to monitor the progress of the study which was previously approved; not only for the changes but to ensure continued protection of the rights and welfare of research subjects.

PI/Co-I/CTC must submit continuing review report/annual report to the IEC annually, subsequent to the date of IEC approval to renew approval before two months of expiry.

All information must be provided to IEC, as requested in the continuing review application form (Refer IEC SOP)

The Investigator/CTC should submit the continuing review application well in advance i.e. 10 months after IEC final approval.

CTC should submit three hard copies of the report (1+2) and a soft copy.

CTC should obtain a copy of the annual/continuing review report acknowledged by IEC, and file the same in TMF and send a copy to sponsor (via email/fax).

The IEC, Secretariat will notify Principal Investigator in case committee recommended modifications, and PI will be requested to resubmit the relevant documents within 1 month for the approval till then the project is suspended. Principal Investigator will be communicated about the decision within 14 working days after the minutes are finalized.

The PI will receive a letter from IEC, if the continuing review report/annual report is approved / accepted.

The letter should be file in the TMF and a copy should be provided to the sponsor.

*Note: If there is delay in approval of the continuing review report subsequently from the date of IEC approval, the PI cannot recruit any patient during that phase, till IEC/, approve the continuing review report.*

4.3.2.5 Study Termination

a. Premature Termination / Suspension /Discontinuation of the study

Research studies are usually terminated as per the recommendation of the IEC, PI, Sponsor or other authorized bodies wherein subject enrollment and subject follow-up are discontinued before the scheduled completion of the study.

The IEC/Sponsor/PI/ other authorized bodies can prematurely terminate the study for the following reason but not limited to:

Protocol non-compliance/violation due to any reason. o Slow recruitment

Frequency of SAEs occurring at trial site may require the study to be prematurely terminated for the safety of the patients.

Sponsor find treatment ineffective

Lack of funds, lack of adequate market potential, competing drugs have received marketing approval ahead of the test compound, etc.

Overall trial enrollment was met, so all sites are being closed, even if some sites have not completed their enrollments.

Based on the above mentioned reasons IEC secretary can send a notification letter for termination/suspension/discontinuation or query letter to request additional information to the PI.

In case Sponsor is terminating the study, PI will receive a letter from Sponsor/CRO for the termination/suspension/discontinuation with the explanation for the same.

PI and CTC will prepare the protocol termination package along with covering letter, Premature Termination Report signed and dated by PI and another material (e.g. letter received from the Sponsor/PI/IEC)

The CTC must obtain acknowledgment of the IEC member on the covering letter and file it in the TMF.

PI/CTC must reply immediately in case of any query generated or any further information requested from the IEC.

The PI will receive acceptance letter from the IEC, CTC will keep the original letter of the Premature Termination/suspension/discontinuation report in the study file and send the file to archive (Refer SOP; Archival of Essential Documents). Inform the same to Sponsor/CRO.

**4.3.2.6 Study completion**

On the Study completion the PI/ CTC will notify the IEC of the study completion using the study completion form. Additionally the PI and CTC must submit letter provided by the sponsor/CRO to give adequate and sufficient information.

The CTC must submit one hard copy + soft copy of Study Completion Reports Note: One additional copy for PI Acknowledgement

IEC may call PI and request for further information or take any other action. In case, further information / action are requested, the same should be followed by the PI and communicated to the IEC office within 30 days.

After providing the information requested by the IEC, PI may receive acceptance letter from IEC.

IEC acceptance letter will be filed. One copy must be send to Sponsor/CRO.

**4.4 Applicable Staff**

This SOP applies to all the personnel of the clinical research team and others who may be responsible for the interaction with the IEC.

These include the following:

* Investigator
* Research Team (listed in the delegation log)
* CTC
* IEC staff/members

**4.5 Staff responsible for Implementation**

Clinical Research staff and Investigators will ensure that the research team involved in the conduct of the study will comply with this site SOP.

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

**References**

1. 21 CFR 312.60 – General Responsibilities of Investigators

2. Guideline Good Clinical Practice

3. ICH Guidelines for Good Clinical Practice (E6)

4. ICH Guidelines for Good Clinical Practice (E6) section 3.1 – Responsibilities

5. ICH Guidelines for Good Clinical Practice (E6) section 4.10 – Progress Reports

6. ICH Guidelines for Good Clinical Practice (E6) section 4.11 – Safety Reporting

7. ICH Guidelines for Good Clinical Practice (E6) section 4.12 – Premature Termination of Suspension of a Trial

8. ICH Guidelines for Good Clinical Practice (E6) section 4.13 – Final Reports by Investigator / Institution

9. ICH Guidelines for Good Clinical Practice (E6) section 4.4 – Communication with IEC/IEC

10. ICH Guidelines for Good Clinical Practice (E6) section 5.21 – Premature Termination or Suspension of a Trial

11. Schedule Y : Responsibility of Investigator