STANDARD OPERATING PROCEDURE [SOP 7]

Monitoring of Research Projects

Table of contents		
Sr. No.	**Content**	**Page No.**
1	Purpose	1
2	Scope	1
3	Monitoring participant's rights, safety and wellbeing	1
4	Safeguarding Vulnerable Population	3
5	Ensuring adequacy and continuity of consent process	4
6	Conduct of For-cause assessments following non-compliance and/or complaints for the trials approved by the ethics committee	5
7	Identifying opportunities for improvement and actions to be initiated	5

1. Purpose

The purpose of this standard operating procedure (SOP) is to describe the procedures for continuous monitoring of the approved research projects by the Institutional Ethics Committee-CHARUSAT.

2. Scope

This SOP applies to all IEC-CHARUSAT approved studies for which a routine or for-cause on-site monitoring may be undertaken by the IEC-CHARUSAT.

3. Monitoring participant's rights, safety and well being

It will be the responsibility of the Entire Committee to decide and conduct continuous monitoring of an approved research project. It will be further the responsibility of the designated IEC-CHARUSAT member(s) to perform on-site monitoring of selected study site(s).

A. Selection of study sites

Routine monitoring for a site may be decided at the time of approval of the project by the entire committee. This may be recorded in the IEC-CHARUSAT decision and in the IEC-CHARUSAT minutes of the meeting.

B. Before the visit

Irrespective of the reasons for conducting monitoring, the following procedure will be followed:

a. The Chairperson will identify and select one or more IEC-CHARUSAT members (henceforth referred to as monitors) to conduct monitoring of a site.

b. The agenda of monitoring will be decided by the identified monitors in consultation with the Member Secretary and Chairperson

c. The Member Secretary will decide the date of the monitoring in consultation with the monitors and the PI.

d. The final date will be communicated to the PI (with a request to be available) and monitors.

e. The Member Secretary will provide Monitors with relevant reference material / documents related to the project for review.

f. Monitors will carry with them Site Monitoring Visit Report Forms from IEC-CHARUSAT Office for documentation of the monitoring findings.

C. During the visit

The Monitor will follow the check list and will:

a. Check the log of delegation of responsibilities of study team, check if the site is using latest IEC-CHARUSAT approved current versions of the protocol, informed consent documents, case record forms, diaries, advertisements, etc.

b. check investigational product accountability is adequately controlled and documented throughout the product flow at the study site (arrival, dispensing, use, return from the subject and return/destruction after the study),

c. check for storage times, conditions and expiry dates to be acceptable and sufficient supplies available, wherever applicable,

d. verify that the investigator follows the approved protocol and all approved amendment(s), if any,

e. ensure that the investigator and the investigator's trial staff are adequately informed about the trial,

f. verify that the investigator and the investigator's trial staff are performing the specified study functions, in accordance with the approved protocol and any other written agreement between the sponsor and the investigator/institution, and have not delegated these functions to unauthorized individuals,

g. verify that the investigator is enrolling only eligible subjects, [1st as well as subsequent ones from recruitment log],

h. Determine whether all Serious Adverse Events (SAEs) are appropriately reported within the time as per the applicable regulatory requirement(s). Case record forms would be checked to review the safety data i.e. Adverse Events (AEs) and SAEs for the volume or severity of adverse events,

i. review the project files of the study to ensure that documentation is filed appropriately,

j. review the source documents for their completeness,
k. check for unreported protocol deviations or violations,

The Monitor will fill the Site Monitoring Visit Report Form, sign and date it.

[Annexure 10]

4. Safeguarding Vulnerable Population

IEC-CHARUSAT identifies vulnerability of participants in human research and takes all necessary steps to safeguard their volunteer participation and safety, with special focus on women, Pregnant Mothers, Children, and Geriatric Population etc.

Individuals may be considered to be vulnerable if they are,

1. Socially economically disadvantaged and therefore susceptible to being exploited;
2. In capable of making a voluntary informed decision for themselves or whose autonomy is compromised temporarily or permanently, for example people who are unconscious, differently abled;
3. Able to give consent, but whose voluntariness or understanding is compromised due to their situational conditions; or
4. Unduly influenced either by the expectation of benefits or fear of retaliation in case of refusal to participate which may lead them to give consent.

Principles of research among vulnerable population

1. Vulnerable population have an equal right to be included in research so that benefits accruing from the research apply to them as well.
2. If any vulnerable group is to be solely recruited then the research should answer the health needs of the groups.
3. Participants must be empowered, to the maximum extent possible, to enable them to decide by themselves whether or not give assent/consent for participation.
4. In vulnerable population, when potential participants lack the ability to consent, a LAR should be involved in decision making.
5. Special care must be taken to ensure participant's privacy and confidentiality, especially because breach of confidentiality may lead to enhancement of vulnerability.

6. If Vulnerable population are to be included in research, all stakeholders must ensure that additional protections are in place to safeguard the dignity, rights, safety, and well being of these individuals.

Additional safeguards/protection mechanisms

When vulnerable individuals are to be recruited as research participants additional precaution should be taken to avoid exploitation/retaliation/reward/credits, etc., as they may either feel intimidated and incapable of disagreeing with their caregivers, or feel a desire to please them. In the first case, they may be subjected to undue pressure, while in the second, they may be easily manipulated. If they perceive that their caregivers want them to participate in research, or if the caregiver stands to benefits from the dependant's participation, the feeling of being pressed to participate may be irreversible which will undermine the potential voluntariness.

1. Researcher must justify the inclusion of a vulnerable in the research.
2. IEC-CHARUSAT must satisfy them with the justification provided and record the same in the proceedings.
3. Additional safety measures should be strictly reviewed and approved by IEC-CHARUSAT.
4. The informed consent process should be well documented. Additional measures such as recording of assent and re-consent, when applicable, should be ensured.
5. Research on sensitive issues such as mental health, sexual practices/preferences, HIV/AIDS, substance abuse, etc may present special risks to research participants.
6. Researchers should be cognisant of the possibility of conflicting interests between the prospective participant and LAR and should be more careful.

4. Ensuring adequacy and continuity of consent process

The monitor will:

a. observe the informed consent process, if possible,
b. review randomly selected participant's files to ensure that participants are signing the correct informed consent
c. may even interview, if participant is available

[Annexure 22,23]

5. Conduct of For-cause assessments following non-compliance and/or complaints for the trials approved by the ethics committee

"For-cause monitoring" will be performed at sites for reasons identified by any member of the IEC, after approval by the Chairperson. The reasons for identifying a particular site for "for-cause monitoring" could include any one or more of the following:

a. High number of protocol deviations/ violations

b. Repeated Adverse Event (AE)/ Serious Adverse Events (SAE) reports in a trial

c. Too many SAEs for a particular investigator over a period

d. High recruitment rate

e. High number of instances requiring active observation

f. Complaints received from participants or any other person

g. Frequent failure to submit the required documents

h. Any other cause as decided by IEC-CHARUSAT

6. Identifying opportunities for improvement and actions to be initiated

A. After the on- site visit by the monitor

i. The Monitor will submit the completed Site Monitoring Visit Report Form to the IEC-CHARUSAT Member Secretary within 7 working days of conducting a site monitoring visit or at the time of full board meeting (whichever is earlier).

ii. The report should describe the findings of the monitoring visit.

iii. The Member-Secretary will present the monitoring report at the next full board IEC-CHARUSAT meeting and the concerned Monitor will provide additional details/ clarifications to members, as required.

iv. The IEC-CHARUSAT will discuss the findings of the monitoring process and take appropriate specific action by voting or combination of actions, some of which are listed below:

1. Continuation of the project with or without changes,
2. Restrictions on enrolment
3. Recommendations for additional training
4. Recruiting additional members in the study team
5. Revising/ providing qualifications/ experience criteria for members of the study team, termination of the study, suspension of the study, etc.

v. The Monitor has findings that impact on safety of the participant, the Monitor will inform the Member Secretary on the same day. The Member Secretary will discuss with the Chairperson to decide on the suitable action to be taken.

vi. The final decision taken at the full board IEC-CHARUSAT meeting by the Chairperson will be recorded in the Site Monitoring Visit Report Form

vii. The Member Secretary will convey the decision to the Principal Investigator in writing within 14 working days of the meeting.

viii. The Member Secretary will place the copy of the report in the protocol file.

B. Measures apart from active monitoring

The Committee can call for and discuss information on any relevant aspect (s) of the project with the investigator (s) at any time. In particular, the Committee may require investigators to provide interim reports on stipulated dates and a final report at completion of the study.

1. The Committee may ask for the following information in the report:

- Progress to date, outcome/ results and publications/ presentations in the case of completed research
- Maintenance, security, confidentiality and integrity of records and data
- Compliance with the approved protocol
- Compliance with any conditions of approval
- Changes to the protocol or conduct of the research
- Changes to the personnel of the PI /other investigators and
- Serious Adverse events or complaints relating to the project

2. The Committee will require, as a condition of approval of each project, that investigators immediately report anything which might warrant review of ethical approval of the protocol, including:

- Proposed changes in the protocol
- Any unforeseen events that might affect continued ethical acceptability of the project new information from other published or unpublished studies which may have an impact on the continued ethical acceptability of the trial, or which may indicate the need for amendments to the trial protocol.

3. The Committee will also require, as a condition of approval of each project, that investigators inform the IEC-CHARUSAT, giving reasons, if the research project is discontinued before the expected date of completion, and that the investigators comply with the approved protocol.

4. The Committee will ensure that adequate information with regards to rights and responsibilities of research participants are displayed at relevant sites too (CHARUSAT website).

5. At the end of each financial year, before preparing its report to the Appointing Authority, the Committee will require all investigators[s], whose projects have been approved in the preceding year, to declare to the Committee, in writing the status of their ongoing research projects