STANDARD OPERATING PROCEDURE [SOP-5]

REVIEW OF RESEARCH PROPOSALS

Table of contents

1. Purpose

The purpose of this standard operating procedure (SOP) is to describe the initial review of research proposals prior to their initiation and regular monitoring of the approved research project to ensure ethical compliance during the conduct of research. By this the committee also ensures to safeguard the dignity, rights, safety and well-being of all research participants.

2. Scope

This SOP applies to all studies submitted to IEC for establishment of an appropriate

and sustainable system for quality ethical review and monitoring.

3. Review by conducting a formal Meeting

All proposals that are submitted to the Institutional Ethics Committee for the review will be thoroughly and critically evaluated and the decision about the proposal will be taken during the Meeting. The Meeting will be considered valid, only if the quorum is maintained throughout the Meeting and at the time of decision making process as well. If the IEC Member has declared a conflict of interest for any research proposal, then a written statement stating the same will be submitted to the Chairperson of the IEC, before beginning of the meeting and shall be recorded in the minutes of the meeting. The member who has declared conflict of interest will be asked to withdraw from the IEC Meeting, i.e. vacating the Meeting venue, while the research proposal is being discussed upon, if he/ she is not an investigator. If the IEC Member is an investigator, he/ she shall be present for review process only. At the time of discussion amongst members and final decision, the concerned member shall leave the meeting. This will be recorded officially and the quorum rechecked. A list of absentee members as well as members leaving or entering in-between the meeting will also be recorded. Proposals will be taken up item-wise, as given in the agenda. Number of proposals reviewed in a meeting will justify that there is ample time devoted for review of each proposal. If there is more number of proposals for consideration per meeting, the meetings will be arranged frequently to review them. The time allotted for the meeting will be reasonable to allow ample discussion on each agenda item. The minutes of the previous meeting and list of protocols that underwent expedited review will be ratified. The contents of the patient/participation information sheet including the local language translations, back translations of the informed consent document in English, wherever required; provision for audio- visual recording of consent process, if applicable, as per relevant regulations; and if consent waiver or verbal/oral consent request has been asked for, this will be specifically reviewed.

Apart from research proposals taken for Full Committee/ Board Meeting, investigator[s] can submit their research projects any time to the IEC, in the same way as

mentioned above, with justification as to why their research project should be considered for an expedited review.

Project[s] will be considered eligible for Expedite Review where they involve:

a. Minor amendments and extensions of approved protocols

b. Urgent amendments to approve protocols for safety reasons

c. Urgent proposal of the National interest

d. Research on interventions in emergency situations, such as epidemic or pandemic

e. Research on Disaster Management.

Few examples that may be eligible for Expedited Review:

- Revised proposal with minor modifications, which were previously approved through full review by the IEC
- Change in the Name and/ or address of the sponsor
- Change in the contact details of Principal Investigator and/ or Member-Secretary, IEC
- Request to change Principal Investigator[s], Co-Investigator[s]or any member involved in the research.
- Minor corrections in the budget
- Other administrative changes in the investigator brochure, informed consent document etc.

Expedited Review[s] of the research projects may be undertaken between scheduled meetings at the discretion of the Member Secretary, IEC depending upon the need. The Member Secretary, IEC will be free to seek advice from other IEC Members or suitably qualified experts, as appropriate [usually 2-3 Members/ Experts], before reaching to a decision. Any research that is deemed to have potential risk/ raises ethical issue after such expedite review may be slotted for a generous review in the next full committee meeting and the decision of the same will be communicated to the investigator, in hard as well as soft copy. Methodology to conduct the meeting, review procedure, noting of the minutes and communication with the PI will remain same as stated above (or 'mentioned earlier in this document'). The decision and the minutes of the review will be noted down

for ratification at the next IEC meeting.

Any research with the potential for physical or psychological harm to the trial participant will generally not be considered for the expedited review. This includes, and is not limited to, regulated clinical trials, research involving invasive physical procedures and research exploring sensitive personal or cultural issues. In case any research involves a violation of the ethical principles of integrity, respect and privacy of the participant[s],and beneficence and justice, the protocol will be considered in the Full Committee/ Board Meeting and will not be considered for the Expedited Review.

[Annexure 5, 5.1]

4. Initial review of the proposed clinical trial

The IEC members will undergo initial and continuing training in the Human Research Protection, IEC SOPs and related regulatory requirements. All the training details will be documented. The IEC will perform its function through competent initial and continuing review of all scientific, ethical, medical and social aspects of research proposals received in an objective, timely and independent manner by attending meetings, participation in discussion and deliberations. Only the full committee will do initial and continuing review of such proposals. The IEC may have empowered representatives from the specific populations during deliberations. Meetings of IEC shall be held on scheduled intervals as prescribed (once in 2 Months, for which the dates may be finalized at the end of the previous meeting). Additional meetings may be arranged as and when necessary, especially in case of reported adverse events (AE) and/ or serious adverse events (SAE) and for the Expedite Reviews. Last date for receipt of new research proposals shall ordinarily be 2 weeks prior to the scheduled meeting but never less than 1 week. Projects need to be submitted in hard copy or soft copy where feasible, a hard copy [master file] of the complete proposal needs to be submitted to the IEC Office too. On receipt of the hard copy and as oft copy, the IEC Coordinator shall forward the project[s] to the Member Secretary. After the MS review it for completion of the submitted documents, he/ she shall forward the project to all the members. About 2 weeks' time shall ~~be~~ ordinarily be given to each member to review the project. In case where a subject expert is needed, it shall be identified from already available pool of experts

[within/ outside the institution] and the documents of the project shall be forwarded to him/ her. Primary reviewers may be identified for reviewing specific components of a given research proposal.

After initial review of the project, all the members shall send their comments/ suggestions to the Member Secretary. Upon receiving the suggestions from all the members, the MS shall later prepare a consolidated suggestion sheet, which shall be forwarded to the Principal Investigator within stipulated time.

PI will be available during the meeting and will be invited to offer clarifications, if required. The decisions will be taken by consensus after thorough discussions and critical evaluation. Voting may be performed, if necessary. If a decision is reached by the voting process, specific comments on the minority votes shall specifically be included in the minutes of the meeting. The decisions of the meeting shall be recorded in the minutes of the meeting. Later, it shall be circulated via email to all the members for suggestions or corrections, to be replied within a stipulated time frame. On receiving replies from all the members, MS shall further finalize the minutes of the meeting and communicate it to the Chairperson for the signature and approval. The minutes of meeting shall be archived as a separate file and confirmed during the next meeting.

[Annexure 17, 18]

5. Review of the informed consent document, the assent form (as applicable) and translations

The informed consent process will be reviewed by considering following points:

- The process used for obtaining informed consent, including the identification of those responsible for obtaining consent and the procedures adopted for vulnerable populations;
- The adequacy, completeness and understandability of the information to be given to the research participants, and when appropriate, their LARs;
- Contents and details of the patient/participation information sheet including the local language translations;
- Back translations of the informed consent document in English, wherever required;
- Provision for audio-visual recording during the informed consent process, if applicable, as per relevant regulations;

- If consent waiver or verbal/oral consent request has been asked for, this will be reviewed by assessing whether the protocol meets the criteria or not.

[Annexure 16]

6. Review of the informed consent processes

In a reviewed research project, verbal/oral consent/waiver of consent/re-consent may be obtained under certain conditions after due consideration and approval by the IEC. It is the responsibility of the IEC to review and approve a request for verbal/written consent waiver. The Member Secretary will record this decision in the minutes. If the proposal has undergone expedited review, the waiver of consent will be granted only after full board review. The final decision whether to grant the waiver or not will be taken at a full board meeting, unless the project is considered under the expedited review. Criteria shall be as per the existing ethical guidelines and regulatory requirements. The decision regarding approval / disapproval of waiver will be informed to the Principal Investigator in writing. If the waiver is not granted, the IEC will provide reasons for the same. In certain circumstances, the audio or audio-visual recording of the informed consent process may be required. These shall be approved as per the existing regulatory requirements for the same.

[Annexure 16]

7. Evaluation of the recruitment strategies

The recruitment strategies will be evaluated to ensure equitable inclusion of participants without any skew towards particular patient population with regard to the socio-economic class, gender or literacy. Particular emphasis will be placed on following aspects of the recruitment strategies:

a. The characteristics of the population from which the research participants will be drawn (including gender, age, literacy, culture, economic status, and ethnicity)

b. The means by which initial contact and recruitment is to be conducted

c. The means by which complete information is to be conveyed to the potential research participants or their representatives

d. Inclusion criteria for the research participants

e. Exclusion criteria for the research participants

f. Students or staff recruitment in the research

g. Healthy volunteers

h. Information mentioned in the advertisement and its mode of communication

i. Final copy of the printed advertisements

j. Final audio or video taped advertisements

k. Compensation being provided for travel as well as daily wages on case to case basis

[Annexure 10, 22, 23]

8. Evaluation of the proposals involving a special group and a vulnerable population

The Institutional Ethics Committee will evaluate the specific context-dependent characteristics that may place study participants at increased risk of being harmed or wronged (CIOMS). The IEC will ensure special protections to the groups considered to be vulnerable, including allowing for no more than minimal risks for the research procedures that offer no potential individual benefits for participants, or requiring that the research be carried out only when it targets conditions that affect these groups. The IEC will enable the participation of vulnerable individuals by protecting their rights and interests through certain special safeguards and protections. The Member Secretary with Secretariat will maintain up-to-date tools, such as checklists to review research concerning vulnerable groups based on the new and evolving applicable regulations and guidelines. The IEC Chairperson / Member Secretary will be responsible for ensuring that the IEC members are completely familiar with the new and evolving regulations and guidelines pertaining to the vulnerable populations, through conducting/ organizing regular training programmes. The Chairperson/ Member Secretary will be responsible for selecting primary reviewers with appropriate expertise to conduct the reviews of such research and for securing consulting expertise as and when required for the selected reviews. The IEC member will be responsible to conduct review of the research planned for the vulnerable populations, including an assessment of potential for coercion.

In such research projects, the subject experts from identified pool within the institution or as the case may by specific population groups will be invited for the meeting. The subject expert will be selected from the ones who meet criteria as for specific IEC member mentioned in the IEC composition. They will be asked to submit

confidentiality and conflict of interest document prior to the meeting and shall not have any voting rights.

[Annexure 18]

9. Evaluation of the budget with regards to indemnity, compensation, roles and responsibilities

The IEC will review the proposed plan for tackling any medical injuries or emergencies. The source and means for compensation for study related injury will be ascertained. Plans for payment for participation, reimbursement of incurred costs, such as travel or lost wages, incidental expenses and other inconveniences will also be reviewed. A letter from the HOI shall ……. to take care of research related injuries and their treatment.

The IEC will approve travel costs to tune of Rs. 500/- [from within Anand/Nadiad District] and Rs. 1000/- [from outside Anand District] when the actual travel bills are not available. In case of availability of the actual bills, the actual amount would need to be reimbursed. This would be applicable in cases where patient visit is apart from standard of care.

[Annexure 17, 18]

10. Review of the amendments to the originally approved protocol, consent forms and investigators brochure

a. Post decision communication

After review of any research protocol, the IEC will give one of the following decisions:

- Letter of suggestions – for revision with minor modifications/amendments
- Approval with or without mandatory regulatory instructions [as the case maybe]
    - Approval will be given after examination by the Member Secretary or the expedited review, as the case maybe;
- Revision with major modifications for resubmission
    - This will be placed before the full committee for reconsideration for the approval; or not approved (or termination/revoking of permission if applicable)
- Disapproval/ revoking of permission
    - Clearly defined reasons will be given for not approving/ terminating/

revoking of permission.

b. Amendments submitted

The amendments will be incorporated in the proposal(s) to align to the research needs arising from the emergency including issues related to re-consent from the participants. The IEC will ensure that the clinical trials should be conducted in accordance with the ethical principles described in these guidelines, Indian GCP as well as applicable regulations for medical and medicated devices, that is, GSR 78 (E) dated 31.1.2017 or as per the amendments/modifications issued from time-to-time.

- Any proposed changes to the approved projects will require to be reported by the PI to the IEC for review. All amended documents [submitted in hard as well as soft copies will have the changes highlighted and contain revised version numbers and dates [where applicable]. Additionally, summary of changes outlining the nature of the proposed changes, reasons for the changes, and an assessment of any ethical implications arising from the request on the conduct of the research will also need to be submitted.

- The Expedited Review of requests for the minor amendments and urgent amendments to the approved protocols for safety reasons may be undertaken by the Member Secretary between scheduled meetings at the discretion of the Chairperson [as above], which will be ratified at the next IEC meeting. MS shall ensure that such requests do not hamper patient's safety and fall within the ambit of the IEC mandate for the expedited reviews.
- All other requests for the amendments will be reviewed by the IEC at its next scheduled Full Committee/ Board meeting, provided the request has been received by the Member Secretary by the agenda closing date. The procedure of review of amendment shall remain the same as to be followed for reviewing a new research project.
- The decision of the IEC will be communicated in writing to the PI, advising whether the proposed amendment and/or request for extension has been given ethical approval within 15 working days of the meeting at which the request was considered [this may be the Full Committee meeting or an Expedited Review Meeting].
- Notification of the approval of amendments and extensions will be conveyed in

writing in the standard format as per Schedule Y [as stated above].

- If the IEC determines that further information, clarification or modification is required for the consideration of the request for amendment or extension, the correspondence to the investigator will clearly articulate the reasons for this determination, and will clearly set out the information that is required.
- All received and approved requests for amendments and extensions will be recorded, and the status of the project will be updated in the IEC's data of received and reviewed applications.
- In cases of re-consenting or use of newly updated consent forms, the IEC shall ask for submission of a copy of re-consented document or a copy of newly update consent form.

[Annexure 18]

11. Periodic review of trial

The IEC will review ongoing research at six-month interval (or more often, if deemed necessary depending on the level of risk). It will make sure that the progress report, safety report[s] and the final reports will be submitted at the regular intervals.

- Progress reports:
  - In those cases, where the IEC has requested the submission of progress reports, these will be submitted to the IEC, generally within six weeks of the anniversary of the IEC approval.
  - The progress report consists of a simple declaration notifying the IEC about any ethical problems or adverse events which may have occurred during this period.
- Protocol deviations and violations:
  - In case where deviation/ violation from or changes to the protocol [s] occur, they must be reported by the PI within 15 days of such deviation/violation.
  - Along with its report, it needs to be clearly stated whether such protocol deviation or violation has/ had any impact on participant's safety and what measures have been initiated by the PI to ensure that such deviations or violations are prevented in future.

- Final reports:
  - The IEC will receive a final report as soon as the research gets completed.
  - It would include information on whether the study achieved its objectives, the main findings and arrangements for publication or dissemination of the research including any feedback to the participants.

[Annexure 10]