STANDARD OPERATING PROCEDURE [SOP]

REVIEW OF CLINICAL TRIAL PROTOCOL

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1. Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe what and how the Institutional Ethics Committee (IEC) members will review a new research study protocol, at a formal meeting with use of basic principles of research ethics, autonomy, no harm, beneficence and justice keeping in mind. It will also help committee for critical monitoring post approval including SAEs and grievances of different stakeholders.

2. Scope

This SOP applies to the initial review and assessment of all research study protocols submitted for review and approval from the IEC. All research studies presented for full committee or expedited review are covered in this SOP. Scope will be extended to principles of monitoring and grievance handling.

3. Review of clinical trial protocol

IEC will review and take decision regarding approval of REGULATED research proposals/ trials involving human participants that conform to safeguard the dignity, rights, safety and well-being of all actual and potential research participants. **The goals of research, however important, will never be permitted to override the health and well-being of the research participants.** IEC will take care that all the cardinal principles of ethics viz. autonomy, beneficence, non - maleficence and justice are taken care of in planning, conducting and reporting of the proposed research.

For this purpose, it will look into the aspects of Informed consent process, risk benefit ratio, distribution of burden and provisions for appropriate compensations, wherever required. It will review the proposals before start of the study; once approved, will examine its compliance with all regulatory requirements, applicable guidelines and laws as updated with time and monitor the research throughout the study until and after completion of the study.

The mandate of the IEC will be to review those research proposals that

1. involve participants taken from HMPCMCE institutions
2. are undertaken at HMPCMCE institutions
3. carried out by faculty of HMPCMCE institutions

IEC shall ensure that all research involving human participants is conducted in accordance with the basic and general ethical principles. The researcher and the team shall be responsible for protecting the dignity, rights, safety and well-being of the participants enrolled in the study. They should have the appropriate qualifications and competence in research methodology and should be aware of and comply with the scientific, medical, ethical, legal and social requirements of the research proposal.

Each review will be based on Statement of General Principles as per ICMR Ethical Guidelines for Biomedical Research on Human Participants, 2017. If the case may be that these Guidelines are updated, then the same will be the basis of review, for the period new guidelines are in vogue.

Any research using the human beings as participants will follow the principles given below –

1. **Principles of essentiality**, whereby the research entailing the use of human participants is considered to be absolutely essential after a due consideration of all alternatives in the light of the existing knowledge in the proposed area of research and after the proposed research has been duly vetted and considered by an appropriate and responsible body of persons who are external to the particular research and who, after careful consideration, come to the conclusion that the said research is necessary for the advancement of knowledge and for the benefit of all members of the human species and for the ecological and environmental wellbeing of the planet.

2. **Principles of voluntariness**, informed consent and community agreement whereby research participants are fully apprised of the research and the impact and risk of such research on the research participant and others; and whereby the research participants retain the right to abstain from further participation in the research irrespective of any legal or other obligation that may have been entered into by such human participants or someone on their behalf, subject to only minimal restitutive obligations of any advance consideration received and outstanding. Where any such research entails treating any community or group of persons as a research participant, these principles of voluntariness and informed consent will apply, mutatis mutandis, to the community as a whole and to each individual member who is the participant of the research or experiment. Where the human participant is incapable of giving consent and it is considered essential that research or experimentation be conducted on such Statement of General Principles in Biomedical Research Involving Human Participants a person incompetent to give consent, the principle of voluntariness and informed consent will continue to apply and such consent and voluntariness will be obtained and exercised on behalf of such research participants by someone who is empowered and under a duty to act on their behalf. The principles of informed consent and voluntariness are cardinal principles to be observed throughout the research and experiment, including its aftermath and applied use so that research participants are continually kept informed of any and all developments in so far as they affect them and others. However, without in any way undermining the cardinal importance of obtaining informed consent from any human participant involved in any research, the nature and form of the consent and the evidentiary requirements to prove that such consent was taken, will depend upon the degree and seriousness of the invasiveness into the concerned human participant's person and privacy, health and life generally, and, the overall purpose and the importance of the research. Ethics committee will decide on the form of consent to be taken or its waiver based on the degree of risk that may be involved.
3. **Principles of non-exploitation**, whereby as a general rule, research participants are remunerated for their involvement in the research or experiment; and, irrespective of the social and economic condition or status, or literacy or educational levels attained by the research participants kept fully apprised of all the dangers arising in and out of the research so that they can appreciate all the physical and psychological risks as well as moral implications of the research whether to themselves or others, including those yet to be born. Such human participants should be selected so that the burdens and benefits of the research are distributed without arbitrariness, discrimination or caprice. Each research will include an in-built mechanism for compensation for

the human participants either through insurance cover or any other appropriate means to cover all foreseeable and unforeseeable risks by providing for remedial action and comprehensive aftercare, including treatment during and after the research or experiment, in respect of any effect that the conduct of research or experimentation may have on the human participant and to ensure that immediate recompense and rehabilitative measures are taken in respect of all affected, if and when necessary.

4. **Principles of privacy and confidentiality**, whereby the identity and records of the human participants of the research or experiment are as far as possible kept confidential; and that no details about identity of said human participants, which would result in the disclosure of their identity, are disclosed without valid scientific and legal reasons which may be essential for the purposes of therapeutics or other interventions, without the specific consent in writing of the human participant concerned, or someone authorized on their behalf; and after ensuring that the said human participant does not suffer from any form of hardship, discrimination or stigmatization as a consequence of having participated in the research or experiment.
5. **Principles of precaution and risk minimization**, whereby due care and caution is taken at all stages of the research and experiment (from its inception as a research idea, its subsequent research design, the conduct of the research or experiment and its applicative use) to ensure that the research participant and those affected by it including community are put to the minimum risk, suffer from no known irreversible adverse effects, and generally, benefit from and by the research or experiment; and that requisite steps are taken to ensure that both professional and ethical reviews of the research are undertaken at appropriate stages so that further and specific guidelines are laid down, and necessary directions given, in respect of the conduct of the research or experiment.
6. **Principles of professional competence**, whereby the research is conducted at all times by competent and qualified persons who act with total integrity and impartiality and who have been made aware of, and are mindful of, preferably through training, the ethical considerations to be borne in mind in respect of such research or experiment.
7. **Principles of accountability and transparency**, whereby the research or experiment will be conducted in a fair, honest, impartial and transparent manner after full disclosure is made by those associated with the research or experiment of each aspect of their interest in the research, and any conflict of interest that may exist; and whereby, subject to the principles of privacy and confidentiality and the rights of the researcher, full and complete records of the research inclusive of data and notes are retained for such reasonable period as may be prescribed or considered

necessary for the purposes of post-research monitoring, evaluation of the research, conducting further research (whether by the initial researcher or otherwise) and in order to make such records available for scrutiny by the appropriate legal and administrative authority, if necessary.

8. **Principles of the maximization of the public interest and of distributive justice**, whereby the research or experiment and its subsequent applicative use are conducted and used to benefit all human kind and not just those who are socially better off but also the least advantaged; and in particular, the research participants themselves and or the community from which they are drawn.
9. **Principles of institutional arrangements**, whereby there will be a duty on all persons connected with the research to ensure that all the procedures required to be complied with and all institutional arrangements required to be made in respect of the research and its subsequent use or application are duly made in a bonafide and transparent manner; and to take all appropriate steps to ensure that research reports, materials and data connected with the research are duly preserved and archived.
10. **Principles of public domain**, whereby the research and any further research, experimentation or evaluation in response to, and emanating from such research is brought into the public domain so that its results are generally made known through scientific and other publications subject to such rights as are available to the researcher and those associated with the research under the law in force at that time.
11. **Principles of totality of responsibility**, whereby the professional and moral responsibility, for the due observance of all the principles, guidelines or prescriptions laid down generally or in respect of the research or experiment in question, devolves on all those directly or indirectly connected with the research or experiment including the researchers, those responsible for funding or contributing to the funding of the research, the institution or institutions where the research is conducted and the various persons, groups or undertakings who sponsor, use or derive benefit from the research, market the product (if any) or prescribe its use so that, inter alia, the effect of the research or experiment is duly monitored and constantly subject to review and remedial action at all stages of the research and experiment and its future use.
12. **Principles of compliance**, whereby, there is a general and positive duty on all persons, conducting, associated or connected with any research entailing the use of a human participant to ensure that both the letter and the spirit of these guidelines, as well as any other norms, directions and guidelines which have been specifically laid down or prescribed and which are

applicable for that area of research or experimentation, are scrupulously observed and duly complied with.]

During the review process, the IEC will consider the following elements of a given research proposal:

a. Scientific design and conduct of the study
b. Examination of predictable risks/harms & potential benefits with communication to the study participants
c. Recruitment strategies
d. Procedure for independent selection of subjects in methodology including inclusion/ exclusion, withdrawal, removal criteria and other issues like advertisement details etc.
e. Protection of subject rights and responsibilities
f. Issues related to protocol deviation and violation
g. Management of research related injuries, serious adverse events
h. Payment for participation & Compensation provisions
i. Justification for placebo in control arm, if any
j. Availability of products after the study, if applicable
k. Informed Consent Process [includes participant information sheet, informed consent form in local languages, along with AV recording protocols [where necessary]; Requirement of assent if indicated.
l. Protection of privacy and confidentiality
m. Involvement of the community, wherever required
n. Plans for data analysis and reporting
o. Adherence to all regulatory requirements and applicable guidelines changing from time to time [including CDSCO, GOI, ICMR etc.]
p. Competence of investigators, research and supporting staff
q. Facilities and infrastructure of study sites
r. Criteria for withdrawal of patients, suspending or terminating the study
s. Mechanism declared for trial participant to contact IEC, if need arises
t. Justification for waiver of informed consent
u. Protection of vulnerable population [as stated later]
v. Community need & Social values: Outcome of the planned results should be relevant to the health problem of the society.
w. Disclosure of conflict of interest

[Law of the land will be given absolute preference to any prevailing national or international guidelines

while reviewing any research proposal]

Protection of vulnerable population

1. Vulnerability

- The Council for International Organizations of Medical Sciences (CIOMS) new guidelines [2016] no longer label entire classes of individuals as vulnerable. CIOMS more clearly emphasizes that unless a good scientific reason justifies their exclusion, children and persons who are incapable of giving informed consent must be included in research investigations, provided that appropriate safeguards are in place. Ethics Committees should evaluate the specific context-dependent characteristics that may place study participants at increased risk of being harmed or wronged.
- Just as the definition of vulnerability is context dependent, so is the delineation of special protections. Ethics Committees are expected to devise special protections for groups considered to be vulnerable, including allowing for no more than minimal risks for 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. Ethics committees are expected now to enable the participation of vulnerable individuals by protecting their rights and interests through special safeguards and protections.
- Vulnerable persons are those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests.
- Individuals whose willingness to volunteer in a research study may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate may also be considered vulnerable (WHO).

2. Responsibility

- EC members will identify study proposals including vulnerable participants (population) and ensure that these are considered for full board review.
- EC will ensure that measures for safeguarding rights and interests of vulnerable participants are taken care of in the study proposal. They will ensure that the vulnerable population is not exploited and guide the investigators to design protocols and describe the process of informed consent in such a manner that this will be done.

- EC will see whether the inclusion of vulnerable populations in the study is justifiable or the population is just being exploited to generate clinical data. In such cases, the risk benefit analysis needs to be done critically.
- Effort may be made to ensure that individuals or communities invited for research be selected in such a way that the burdens and benefits of the research are equally distributed:
  - Research on genetics should not lead to racial inequalities.
  - Persons who are economically or socially disadvantaged should not be used to benefit those who are better off than them.
  - Rights and welfare of mentally challenged and differently able persons who are incapable of giving informed consent or those with behavioral disorders must be protected. Appropriate proxy consent from the legally acceptable representative should be taken after the person is well informed about the study, need for participation, risks and benefits involved and the privacy and confidentiality procedures. The entire consent process should be properly documented.
  - Adequate justification is required for the involvement of participants such as prisoners, students, subordinates, employees, service personnel etc. who have reduced autonomy as research participants, since the consent provided may be under duress or various other compelling reasons.
  - Persons, who are terminally ill, have incurable disease and mental illness.
- Before undertaking research/trial in children the investigator must ensure that:
  - Children are not involved in research that could be carried out equally well with adults.
  - The purpose of the research is to obtain knowledge relevant to health needs of children. For clinical evaluation of a new drug the study in children should always be carried out after the phase III clinical trials in adults. It can be studied earlier only if the drug has a therapeutic value in a primary disease of the children.
  - A parent or legally acceptable representative of each child has given proxy consent.
  - The assent of the child should be obtained to the extent of the child's capabilities such as in the case of mature minors from the age of 7 years up to the age of 18 years.
  - Research should be conducted in settings in which the child and parent can obtain adequate medical and psychological support.
  - Interventions intended to provide direct diagnostic, therapeutic or preventive benefit for the individual child participant must be justified in relation to anticipated risks involved in the study and anticipated benefits to society.

- The child's refusal to participate in research must always be respected unless there is no medically acceptable alternative to the therapy provided/ tested, provided the consent has been obtained from parents/ guardian.
- Interventions that are intended to provide therapeutic benefit are likely to be at least as advantageous to the individual child participant as any available alternative interventions.
- The risk presented by interventions not intended to benefit the individual child participant is low when compared to the importance of the knowledge that is to be gained.

➢ As a general rule, pregnant or nursing women should not be participants of any clinical trial except such trials as are designed to protect or advance the health of pregnant or nursing women or fetuses or nursing infants, and for which women who are not pregnant or nursing would not be suitable participants.

- The justification of participation of these women in clinical trials would be that they should not be deprived arbitrarily of the opportunity to benefit from investigations, drugs, vaccines or other agents that promise therapeutic or preventive benefits. Example of such trials are:
  - To test the efficacy and safety of a drug for reducing perinatal transmission of HIV infection from mother to child
  - Trials for detecting fetal abnormalities and for conditions associated with or aggravated by pregnancy etc.
- Women should not be encouraged to discontinue nursing for the sake of participation in research and in case she decides to do so, harm of cessation of breast-feeding to the nursing child should be properly assessed except in those studies where breast feeding is harmful to the infant. Compensation in terms of supplying supplementary food such as milk formula should be considered in such instances.
- Only consent of the women should be mandatory and no proxy consent/ refusal allowed.
- Research related to termination of pregnancy:
  - Pregnant women who desire to undergo Medical Termination of Pregnancy (MTP) could be made participants for such research as per The Medical Termination of Pregnancy Act, GOI, 1971.
- Research related to pre-natal diagnostic techniques:
  - In pregnant women such research should be limited to detect the fetal abnormalities or genetic disorders as per the Pre Conception and Prenatal

Diagnostic Techniques (Regulation and Prevention of Misuse) Act, GOI, 1994 and not for sex determination of the fetus.

4. Rights and responsibilities of participant

The committee shall ensure that all potential clinical trial participants are aware of their rights and responsibilities. For the same, a board in both English as well as Local Language shall be displayed at clinical trial sites where consenting process is done. In order to ensure that rights and responsibilities are protected, IEC shall review Informed Consent Document to see that participant is well informed. Apart from this, IEC shall regularly monitor ongoing trial to oversee protection of rights and responsibilities of the participant.

RIGHTS OF PARTICIPANTS IN A RESEARCH

A] What should you know about trial regulation?

1. Every research/ trial is undertaken only after due approval from competent government authorities and a local Institutional Ethics Committee made up of scientists, doctors, advocates and community members.
    a. These committees ensure that trial participants are exposed to the minimum possible risks and that the risks associated with the trial are reasonable in relation to the expected benefits.
    b. All participants need to be informed about the Institutional Ethics Committee details and are free to approach it for any grievance related to research/ clinical trial
2. To further ensure the safety of participants, a Data Safety Monitoring Board (DSMB) is commonly used.
    a. The DSMB is an impartial group that monitors the progress of clinical trials.
    b. They are not involved in the conduct of the trial but ensure patient safety by analyzing the safety and effectiveness of the experimental treatment periodically during ongoing trial.
    c. They can terminate a trial if expected risk-benefit ratio is not being achieved.

B] What should you know about trial before consenting to participate in research?

1. Rights of Participants of research/ clinical trials are protected under law when participating in clinical trials.

2. The informed consent process is one of the key aspects of protecting research participants and decision to volunteer for a study is individual and free from undue influences. Before consenting to participate in clinical trial, potential participants are expected to
    a. Understand all the possible benefits and risks involved
    b. Understand duration and overall conduct of the study including follow up plan
    c. Understand what will be expected of you as a participant
    d. Understand what will happen if trial is over or in case of a drop out or if discontinued by the investigator
3. The participant has the right to know everything that is going to happen in a study.
    a. He can ask any question and express all concerns about participation in the study
4. The potential participant has the right to refuse to take part in research without affecting his right to get due medical treatment [without prejudice or loss of future treatment].
    a. Participant is also free to withdraw from the study at any time without giving any reason and without having any effect on future treatment
5. During the research/ trial, the privacy of participants and the confidentiality of their data are maintained.
6. If new benefits, risks or side effects are discovered during a study, you will be informed about the same by investigator

RESPONSIBILITIES OF PARTICIPANTS IN A RESEARCH

- To adhere to taking the trial medication according to the prescribed dosages and schedule
- To undergo periodic investigations/ follow up as prescribed in trial protocol on schedule
- To immediately report any observation/untoward event (possible side effect) during the trial

5. Voluntariness and prior intimation with regards to participant's involvement and withdrawal from the trial

IEC shall ensure that no participant is forced to enter into a clinical trial. The informed consent document shall clearly indicate voluntariness for the trial and any refusal shall not have any effect on the ongoing medical treatment. EC shall also review the recruitment procedure, vulnerability and reimbursements decided, which shall also be part of the regular monitoring process. IEC will ensure that each participant is aware of the following:

- Only, to withdraw him/herself from the study at any point of time without affecting his / her ongoing medical treatment as part of standard of care.

- He / she is educated about the predefined conditions or risk analysis when investigators may remove participants from the study. He / she is given chance for re-consenting whenever risk benefit analysis changes due to change in protocol or reports of AE/SAEs or interim review results have achieved the desired outcome or there is increased risk.

[Annexure 5.2, 5.3, 16]

6. Information and comprehension of participants regarding (initial and ongoing) the associated risks and benefits of the trial

Benefits to the individual, community or society refer to any sort of favourable outcome of the research, whether direct or indirect. The social and scientific value of research should justify the risk, which is the probability of causing discomfort or harm anticipated as physical, psychological, social, economic or legal. The researcher, sponsor and EC shall attempt to maximize benefits and minimize risks to participants so that risks are balanced to lead to potential benefits at individual, societal and/or community levels.

To ensure the same, EC shall assess the inherent benefits and risks, ensure a favourable balance of benefits and risks, evaluate plans for minimizing the risk and discomfort and decide on the merit of the research before approving it. As a part of continuing review at appropriate interval and focused review based on notifications of SAEs at the study site or other study sites when notified, EC will also assess any altered risks in the study. For the same, a predetermined checklist shall be used by the members while reviewing research protocol especially informed consent document.

[Annexure 5.2, 5.3, 16]

7. Protection of confidentiality and privacy of participants

Privacy is the right of an individual to control or influence the information that can be collected and stored and by whom and to whom that information may be disclosed or shared. Confidentiality is the obligation of the researcher/research team/organization to the participant to safeguard the entrusted information. It includes the obligation to protect information from unauthorized access, use, disclosure, modification, loss or theft. The researcher should safeguard the confidentiality of research related data of participants and the community.

Potential limitations to ensure strict confidentiality must be explained to the participant. Researchers must inform prospective participants that although every effort will be made to protect privacy and ensure confidentiality, it may not be possible to do so under certain circumstances. Any publication arising out of research should uphold the privacy of the individuals by ensuring that

photographs or other information that may reveal the individual's identity are not published. A specific re-consent would be required for publication, if this was not previously obtained.

EC team will be taking special note on this aspect while going on site visit and interim review. Some information may be sensitive and should be protected to avoid stigmatization and/or discrimination (for example, HIV status; sexual orientation such as lesbian, gay, bisexual, and transgender (LGBT); genetic information; or any other sensitive information). While conducting research with stored biological samples or medical records/data, coding or anonymization of personal information is important and access to both samples and records should be limited.

Data of individual participants/community may be disclosed in certain circumstances with the permission of the EC such as specific orders of a court of law, threat to a person's or community's life, public health risk that would supersede personal rights to privacy, serious adverse events (SAEs) that are required to be communicated to an appropriate regulatory authority etc.

[Annexure 5.2, 5.3, 16]

8. Monitoring to ensure equitable selection of subjects, with special attention to vulnerable and high risk subjects

Efforts must be made to ensure that individuals or communities invited for research are selected in such a way that the benefits and burdens of research are equitably distributed. Vulnerable individuals/groups should not be included in research to solely benefit others who are better-off than themselves. Research should not lead to social, racial or ethnic inequalities. Plans for direct or indirect benefit sharing in all types of research with participants, donors of biological materials or data should be included in the study, especially if there is a potential for commercialization. This shall be decided a priori in consultation with the stakeholders and reviewed by the EC. Any advertisement or leaflet inviting the participants, if there, will be reviewed by the EC.

While regular site visit monitoring by EC and time to time review of ongoing projects recruitment log will be checked to confirm the equitable distribution of participants.

[Annexure 10, 10.1, 22, 23]

9. Compensation for participation in the trial

Payment for participation: Participants shall be reimbursed for expenses incurred relating to their participation in research, such as travel related expenses. Participants shall also be paid for inconvenience incurred, time spent and other incidental expenses in either cash or kind or both as deemed necessary (for example, loss of wages and food supplies). Participants will not be made to pay for any expenses incurred beyond routine clinical care and which are research related including

investigations, patient work up, any interventions or associated treatment. This is applicable to all participants, including those in comparator/control groups. If there are provisions, participants may also receive additional medical services at no cost.

When the LAR is giving consent on behalf of a participant, payment shall not become an undue inducement and will be reviewed carefully by the EC. Reimbursement will be offered for travel and other incidental expenses incurred due to participation of the child/ward in the research. ECs will review and approve the payments (in cash or kind or both) and free services and the processes involved, and also determine that this does not amount to undue inducement. Once approved, EC will look for documents verifying that participants actually got the reimbursement [s].

Compensation for research-related harm: Research participants who suffer direct physical, psychological, social, legal or economic harm as a result of their participation are entitled, after due assessment, to financial or other assistance to compensate them equitably for any temporary or permanent impairment or disability. In case of death, participant's dependents are entitled to financial compensation. IEC shall ensure that the research proposal has an in-built provision for mitigating research related harm.

[Annexure 14, 15]

10. Addressing Serious adverse events as per applicable rules and regulations

- The researcher shall be responsible for reporting all SAEs to the EC within 24 hours of knowledge. Reporting of SAE may be done through email on non-working days. A report on how the SAE was related to the research must also be submitted within 14 days. IEC will also be responsible for reviewing the relatedness of the SAE to the research, using either WHO Causality Assessment Criteria or Naranjo Scale as reported by the researcher, and determining the quantum and type of assistance to be provided to the participants. For clinical trials under the purview of CDSCO, the timeline and procedures as notified from time to time may be followed.
- While deliberating on the quantum of compensation to be awarded to participants who have suffered research-related injury, the EC shall consider aspects including the type of research (interventional, observational, etc.), extent of injury (temporary/permanent, short/long term), loss of wages, etc. All AEs will be recorded and reported to the EC according to a pre-planned timetable, depending on the level of risk and as recommended by the EC.

[[Annexure 19]

11. Compensation for injury as per the rules and regulations with monitoring for noncompliance

The compensation amount in case of trial related injury [if deemed necessary] will be determined based on the guidelines provided by CDSCO as available at:

a. Formula to determine the quantum of compensation in case of clinical trial related serious adverse events [SAE] of deaths occurring during clinical trials: http://www.cdsco.nic.in/writereaddata/formula2013SAE.pdf
b. Formula to determine the quantum of compensation in case of clinical trial related injury [other than death]: http://www.cdsco.nic.in/writereaddata/ORDER%20and%20Formula%20to%20Determine%20the%20quantum%20of%20compensation%20in%20the%20cases%20of%20Clinical%20Trial%20related%20serious%20Adverse%20Events(SAEs)%20of%20Injury%20other%20than%20Death.pdf

The IEC report to CDSCO with regards to evaluation of any trial related/ unrelated serious adverse event shall specifically include that final decision of the Expert Committee, CDSCO be intimated to IEC also. In addition, the Principal Investigator, through Sponsor shall ensure that a copy of acknowledgment of compensation been paid to participant or LAR also be submitted to IEC for record purposes.

12. Addressing complaints and concerns of subjects

- The IEC requires, as a condition of approval of each project, that the investigator immediately report to it any concerns or complaints received with regards to the ongoing approved research project.
- The IEC shall also review complaints and concerns from trial participants.
- The Member Secretary will be the nominated person to receive such concerns and complaints from investigator as well as participants in research or members of the public about the conduct of projects approved by the IEC. He will be responsible for obtaining, in writing, the grounds of the concern or complaint that will be notified to the Chairperson, as soon as possible.
- Upon receipt of such complaint, Member Secretary will acknowledge to the complainant outlining the mechanism for investigating the concern or complaint.
- The Chairperson will examine the concern or complaint and determine whether the concern or complaint warrants a further investigation or not. Where there is to be no further investigation deemed necessary, the Chairperson will inform the complainant, through Member Secretary in writing about the same. All the members will be intimated of such episodes in the next Full

Committee/ Board Meeting and included in the Minutes of the Meeting too.

- Where the Chairperson determines that the concern or complaint warrants a further investigation, he/ she will notify the Head of the Institution of the same. He shall then form a Review Committee to investigate and determine the consequences. This committee would include EC Chairperson, Member Secretary, one EC member designated by Chairperson and one Subject Expert [where required].
- The Member Secretary will then issue a letter of notification to the PI of the concern or complaint about the project received by the IEC outlining the mechanism for investigating the concern or complaint. Where the complaint concerns the conduct of the any other person, Committee will also notify that person too.
- Clarification or answer from the Principal Investigator will be sought on the raised issue. If warranted, surprise research site visit may also be arranged by the members of EC.
- The Review Committee will immediately go for an investigation into the concern or complaint. The investigation will not take longer than 2 weeks from the time of notification for the concern or complaint to be addressed, unless exceptional circumstances exist.
- The Review Committee will give the complainant and the PI an opportunity to make submissions. Where the complaint concerns the conduct of any other person, the Review Committee will also provide that person with an opportunity to make submissions.
- The Review Committee may seek any other information it requires and may access any documents relating to the project, interview other people, and seek internal and external expert advice, as it sees fit.

Consequences

- The Review Committee will meet in person and if it is satisfied that the concern or complaint is justified, it will determine the consequences by considering the following matters:
    a. Severity of the matter
    b. Sensitivity of any information concerned including the amount and type of information and the level of identifiability
    c. Whether any breach of the approved protocol, which may be established, was inadvertent, negligent or unintentional
- The possible consequences will include the following:
    a. Noting on the file of the occurrence of the matter;
    b. Increased monitoring of the project;
    c. Counseling on security practices;

d. Amendments to the approved protocol;

e. Reporting the individuals responsible for any breach of ethics to the Head of the Institute, with a complaint of misconduct in the execution of the project;

f. Revoking of approval for the project

- The Chairman, Review Committee will notify the HOI the consequences in writing along with options for an appeal. The Chairman, Review Committee will also notify the Ethics Committee regarding the complaint received, investigation undertaken and the outcome of the investigation in next full committee meeting, which shall be minuted too.
- The IEC will then re-review the ethical approval of any project in the light of the outcome of the investigation of any breach of ethics or justifiable complaint and will notify the responsible PI & HOI if ethical approval for the project is to be revoked.
- The Chairman, Review Committee will also send a written report of the outcome of the investigation and the consequences to the complainant [whosoever] in writing.
- In cases of protocol deviation/ violation reported by the PI, they will be reviewed in the next Full Committee Meeting, unless any such deviation/ violation has a risk on participant wellbeing/ safety.
- In case of a risk on participant wellbeing/ safety, the Member Secretary will convene an Expedite Review Meeting to deal with the reported matter. Procedure for conduct of meeting, review, minutes as well as communication with the PI will remain the same as above.