2021-2022

Clinical Research Ethics Committee (Human Studies)

Standard Operating Procedures

Netaji Subhas Medical College & Hospital
Amhara, Bihta, Patna, (Bihar)- 801106

Prepared by	Reviewed by	Approved by

SOP Prepared by

Name and Designation	Signature with date
Dr. Swarnima Singh Member Secretary (CREC) Assistant Professor, Department of Biochemistry	1/2/2021

SOP reviewed by

Name and Designation	Signature with date
Prof (Dr) Santanu Kumar Tripathi Member (CREC) Academic Dean, Department of Pharmacology	01.02.2021
Prof (Dr) Ashok Saran Member (CREC) Professor and HOD Department of Physiology	1/2/2021

SOP approved by

Name and Designation	Signature with date
Prof(Dr) Arvind Prasad Principal, NSMCH, Bihta, Patna	01/02/2021

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CONTENTS

I. Short Title:

The following may be called as "Standard Operating Procedures for the Clinical Research Ethics Committee (CREC) of Netaji Subhas Medical College & Hospital, Amahra, Bihta, Patna (Bihar) - 801106.

II. Adoption of SOP:

Netaji Subhas Medical College & Hospital, Amahra, Bihta, Patna (Bihar) herein after referred to as "NSMCH" has adopted these written Standard Operating Procedures (SOP) to ensure the protection of the rights and welfare of human participants in biomedical, experimental and behavioral research conducted at NSMCH.

III. Objective:

The objective of this Standard Operating Procedures of the Clinical Research Ethics Committee (CREC) of Netaji Subhas Medical College & Hospital, Amahra, Bihta, Patna (Bihar) is to maintain effective functioning of the NSMCH-CREC and to ensure quality and technical excellence and consistent ethical review of all the submitted health and biomedical research proposals and ongoing approved research studies involving human participants in accordance with the ICMR ethical guidelines for biomedical research on human subjects.

IV. Authority under which NSMCH-CREC is constituted:

The Principal in consultation with the Managing Director, NSMCH will appoint the Chairperson and all the committee members based on their competence, experience and integrity by sending an official request letter (Annexure 1A & 1B). Members will confirm their acceptance to the Principal by providing all the required information for membership (Annexure 2). The Chairperson will furnish any information or report to the Principal, NSMCH when required.

V. Role and Responsibilities of NSMCH- CREC:

The NSMCH- CREC will review all types of research proposals involving human participants with a view to safeguard the dignity, rights, safety and wellbeing of all actual and potential

research participants before approving the research proposals. The goals of research, however important, should never be permitted to override the health and well being of the research subjects.

The NSMCH- CREC will ascertain whether all the cardinal principles of research ethics viz., Autonomy, Beneficence, Non – malfeasance, Respect for Free and Informed Consent, Respect for Human Dignity, Respect for Vulnerable Persons , Respect for Privacy and Confidentiality 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 protocol review, selection of participants, voluntary participation of potential participants, informed consent process, risk benefit ratio, distribution of burden and benefit, maintenance of privacy and confidentiality and provisions for appropriate compensations. It will review the proposals before the commencement of the study as well as review periodically until the completion of the study through appropriate well documented procedures. Such a review may be based on the periodic study progress reports furnished by the investigators and/or monitoring and internal audit reports furnished by the Sponsor and/or by visiting the study sites.

The mandate of the CREC shall be to review all research projects to be conducted at the Institution involving human beings directly or indirectly, irrespective of the funding agency.

NSMCH- CREC will provide advice to the researchers on all aspects of the welfare and safety of the research participants after ensuring the scientific soundness of the proposed research through appropriate Scientific Review Committee/ Research Committee.

In case an ethics committee revokes its approval accorded to a trial protocol, it will record the reasons for doing so and at once communicate such a decision to the Investigator as well as to the Licensing Authority.

In case of serious adverse event of death occurring to the clinical trial subject, the ethics committee shall forward it's report on the serious adverse event of death, after due analysis, along with its opinion on the financial compensation, if any, to be paid by the Sponsor or his representative, whosoever had obtained permission from the Licensing Authority as defined under rule 21(b) for conducting the clinical trial, to the Chairman of the

Expert committee constituted by the Licensing authority under Appendix XII (gazette notification 30th January 2013) with a copy of the report to the Licensing Authority within twenty one calendar days of the occurrence of the serious adverse event of death. In case of serious adverse event, other than death occurring to the clinical trial subject, the ethics committee shall forward it's report on the serious adverse event after due analysis along with its opinion on the financial compensation, if any, to be paid by the sponsor or his representative, whosoever had obtained permission from the Licensing Authority for conducting the clinical trial, to the licensing authority within twenty one calendar days of the occurrence of the serious adverse event.

Roles and Responsibilities of the CREC

1. The basic responsibility of CREC is to ensure protection of the dignity, rights, safety and well-being of the research participants.

2 .CREC shall ensure ethical conduct of research by the investigator team.

3. CREC is responsible for declaration of conflicts of interest to the Chairperson, if any, at each meeting and ensuring these are recorded in the minutes.

4. CREC shall perform its function through competent initial and continuing review of all scientific, ethical, medical and social aspects of research proposals received by it in an objective, timely and independent manner by attending meetings, participation in discussion and deliberations.

5 CREC shall ensure that universal ethical values and international scientific standards are followed in terms of local community values and customs.

6. CREC should assist in the development and education of the research community in the given institute (including researchers, clinicians, students and others), responsive to local healthcare requirements.

7. Responsibilities of members should be clearly defined. The SOPs shall be given to CREC members at the time of their appointment.

8. The Secretariat should support the Member Secretary and Alternate Member Secretary (if applicable) in all their functions and should be trained in documentation and filing procedures under confidentiality agreement.

9. The CREC should ensure that privacy of the individual and

confidentiality of data including the documents of EC meetings is protected.

10. The CREC reviews progress reports, final reports and AE/SAE and gives needful suggestions regarding care of the participants and risk minimization procedures, if applicable.

11. The CREC should recommend appropriate compensation for research related injury, wherever required.

12. The CREC should carry out monitoring visits at study sites as and when needed.

13. The CREC should participate in continuing education activities in research ethics and get updated on relevant guidelines and regulations.

14. The CREC may see that conduct of same/similar research by different investigators from same institution is harmonized. 'Me too' research (replicative) should not to be encouraged and submission of same research to different funding agencies should not be accepted.

VI. Composition of NSMCH- CREC:

NSMCH- CREC will be a multidisciplinary and multi-sartorial body in composition and independent. The number of members of the Review Board may range from 7 to 15.

The chairperson of the CREC will be from outside the Institution to maintain the independence of the Committee. The Member Secretary will belong to the same Institution and will conduct the business of the Committee. Other members will be a mix of medical / non-medical, legal, scientific and non-scientific persons and may also include members of public to reflect the differed points of view.

There will be representation of age and gender in the Committee to safeguard the interest and welfare of all sections of the society. Member should be aware of local, social and cultural norms, as this is an important social control mechanism. CREC may invite subject experts to take their views, whenever it is needed.

The NSMCH- CREC will include

1. Chairperson

2. Five persons from basic medical science area (One pharmacologist compulsorily, one

Female scientist compulsory)

3. Three clinicians from various Departments

4. Two legal experts or retired judges

5. One social scientist/ representative of non-governmental voluntary agency

6. One philosopher/ Ethicist/ theologian/ Social Worker

7. One lay person from the community

8. Member Secretary

A Sub-Board of the main CREC may review proposals submitted by undergraduate or post-graduate students or if necessary, an Institutional Ethics Committee may be separately constituted for the purpose, which will review proposals in the same manner as described above.

VII. Membership requirements:

1. All members will serve for a period of 3 years on renewable basis. New members will be included in the CREC in such a way that there will be a mix of recently included members and members with some years of experience.
2. During the term, Principal in consultation with the Chairman can disqualify any member if, the contribution is not adequate and/or there is long period of (member) non availability.
3. A member can tender resignation of his office of membership from the CREC to the Principal through the Chairperson after serving one month advance notice.
4. Principal can replace the member of CREC as and when required.
5. Each member is required to sign the declaration and confidentiality agreement regarding CREC activities (Annexure 2)
6. Conflict of interest should be declared by members of the NSMCH- CREC prior to review meeting.

Terms of reference (TOR) for CREC

1.The TOR for the CREC and its members shall be clearly specified by the institution in the SOPs

CREC shall have written SOPs according to which the committee shall function. The CREC shall refer to ICMR guidelines in preparing the SOPs for all biomedical and health research and to CDSCO guidelines for drug and device trials under the purview of the licensing authority. The SOPs shall be updated periodically to reflect changing requirements. A copy of the latest version of SOPs shall be made available to each member and they would be trained on the SOPs. The SOPs will be available in the secretariat of the CREC as both hard and softcopies.

2.The scope, tenure and renewal policy of the CREC should be stated.

3. Members of the CREC should not have any known record of misconduct.
4. The CREC should be registered with the relevant regulatory authorities, for example, ECs approving clinical trials under the ambit of Drugs and Cosmetics Act should be registered with CDSCO.

a. Special situations

i. Institutions can have one or more than one EC. They can have multiple ECs to review large numbers of research proposals. Each EC can function as a stand-alone committee which should follow all the SOPs and TORs of that institution.

ii. An institution that does not have its own EC (user institution) may utilize the services of the EC of another institution (host institution) preferably in the adjoining/near by area. Relevant requirements must be fulfilled before they do so.

Box – 01:Utilizing the services of an CREC by another institution

The following requirements must be fulfilled by institutions that use the services of CREC from another institution:

- The two institutions (host and user) should enter into an MoU for utilizing the services of the EC of the host institution or the user institution should provide a 'No Objection Certificate' and agree to be overseen by the CREC of the host institution.
- The CREC of the host institution should have access to all research records including the source documents and research participants for continuing review of the implemented project, including site visits.
- The CREC of the host institution can undertake site monitoring and will have all the rights and
  Responsibilities related to ethical review of the projects submitted by the user institutions.

Main CREC for the purpose of primary review. This CREC should be located in

1. For multicenter biomedical and health research, all participating sites may decide to

For multicenter biomedical and health research, all participating sites may decide to Utilize the services of one common EC from a participating site identified as designated Main EC for the purpose of primary review. This CREC is located in India and Registered with the relevant authority. However, the local site requirements, such as Informed consent process, research implementation and its monitoring, etc. may be Performed by the local EC. This would require good communication and coordination Between the researchers and EC secretariats of participating sites. For clinical trials under the Drugs and Cosmetics Act, the requirements as stated by CDSCO must be followed.

2. Institutions could have subcommittees such as the SAE subcommittee or expedited review committee. These should be part of the main committee and comprise Chairperson/ Member Secretary and one to two appropriate designated members of the main CERC as defined in the SOPs. These subcommittees can report to the concerned CREC.

a. Terms of reference for CREC members

i. The Principal, in consultation with the Managing Director should appoint all CREC members, including the Chairperson.

ii. The appointment letter issued to all members should specify. The letter issued by the Principal should include, at the minimum, the following:

1. Role and responsibility of the member in the committee
2. Duration of appointment
3. Conditions of appointment

2. Generally, the term of CREC membership may 3 years. The duration could be extended in unexpected situations, with prior approval by the Principal. A defined percentage of CREC members could be changed on a regular basis.

CREC members may be given a reasonable honorarium for attendance at the meeting

3. Members to be appointed on the CREC should be willing to fulfill the CREC requirement as given in box- 02.

Box-02 : Requirements for EC members

Every CREC member must:

1. provide a recent signed CV and training certificates on human research protection and good clinical practice (GCP) guidelines, if applicable;
2. either be trained in human research protection and/or GCP at the time of induction into the EC, or must undergo training and submit training certificates within 6months of appointment (or as per institutional policy);
3. be willing to undergo training or update their skills/knowledge during the irtenure as an CREC member;
4. be aware of relevant guidelines and regulations;
5. read, understand, accept and follow the COI policy of the EC and declare it, if applicable, at the appropriate time;
6. sign a confidentiality and conflict of interest agreement/s;
7. be willing to place her/his full name ,profession and affiliation to the CREC in the public domain; and
8. Be committed and understanding to the need for research and for imparting protection to research participant's in research.

VIII. Quorum requirements:

Minimum of 50% of committee strength + 1 member and not less than 5 members will be required to compose a quorum for the meeting of which at least one member will be from outside the institution, and one member will be a non-scientific member & one from opposite gender. All decisions will be taken in meetings and not by circulation of project proposals (Also Refer Annexure XXV). Quorum will have 5 members with following representations:

(a) Basic medical scientists (preferably one pharmacologist).

(b) Clinicians

(c) Legal expert

(d) Social scientist / representative of non-governmental voluntary agency / philosopher / ethicist / theologian or a similar person

(e) Lay person from the community.

IX. Conduct of NSMCH- CREC meetings:

The Chairperson will conduct all meetings of the NSMCH- CREC. In the absence of the chairperson an alternate Chairperson will be elected from the members by the members present, who will conduct the meeting. The Member Secretary is responsible for organizing the meetings, maintaining the records and communicating with all concerned. He /She will prepare the minutes of the meetings and get it approved by the Chairperson and all the members.

X. Independent consultants:

The NSMCH- CREC may call upon subject experts as independent consultants who may provide special review of selected research protocols, if need be. These experts may be specialists in ethical or legal aspects, specific diseases or methodologies, or represent specific communities, patient groups or special interest groups. E.g. Cancer patients, HIV/AIDS positive persons or Ethics minorities. They will be required to give their specialized views but should not take part in the decision making process which will be made by the members of the NSMCH- CREC.

XI. Application procedures:

1. All proposals should be submitted on any working day 2 weeks in advance of scheduled meeting in the prescribed application form, the details of which are given under "XII Documentation". Copy of SOP of NSMCH- CREC will be given to PI / Co-PI if he/she has applied for review for the 1st time.

2. All relevant documents should be enclosed with application form. (Documents will be available with Member - Secretary, NSMCH- CREC and Institutional Website www.nsmch.com' in the Downloadable section).

3. Required number of copies of the proposal along with the application and documents in prescribed format duly signed by the Principal Investigator (PI) and Co-investigators / Collaborators / Research Scholars shall be guided to the Chairperson NSMCH- CREC, through member secretary. In his/her absence via any person nominated by chairperson. Receipt of the application will be acknowledged by the CREC office.

4. Every application will be allotted a CREC registration number to be used for all future correspondence and reference. The date of NSMCH- CREC meeting will be intimated to the Principal Investigator to attend the meeting and to make a brief presentation of the proposal and to clarify the points raised by the members.

5. The decision of the committee on the proposal will be communicated in writing. If revision is to be made, the revised document in required number of copies should be submitted within a stipulated period of time as specified in the communication or before the next meeting.

6. All research proposals/clinical trials funded/sponsored by Pharmaceutical companies, Agencies, Multinationals etc. will be charged an administrative fee/ processing fee as specified by the Research Secretariat / Office of CREC of NSMCH. Waiver of these fees is permissible for non-funded studies, departmental studies, and studies funded by organizations like ICMR, UGC, DST Government of India, State Science & Technology Department, UNICEF, WHO, USAID. Non Profitable Organizations etc. In general, waiver of administrative fee is possible at the discretion of Chairperson, NSMCH- CREC.

XII. Documentation:

All Research proposals (3 copies along with 1 Soft copy) shall be submitted along with the information and documents as specified in Annexure-3 A, 3 B.

XIII. Review procedures:

(1). the meeting of the NSMCH- CREC will be held on periodic

intervals, i.e. 1st Monday every three months, unless otherwise specified by the member secretary. Additional review meetings can also be held with short notice as and when required. Meetings will be planned in accordance with the need of the work load.

(2). The proposals should be sent to the NSMCH- CREC at least 2 weeks in advance of schedule meeting.

(3). The CREC's member-secretary or secretariat shall screen the proposals for their completeness and depending on the risk involved categorize them into three types, namely, exemption from review, expedited review and full review (explanation is given below).

(4). Decisions will be taken by consensus after discussion, and whenever needed voting will be done. Decision of chairperson will be final.

(5). Researchers will be invited to offer clarifications if need be. The Principal investigator / Research Scholar will then present the proposal in person in the meeting. When the PI is not available due to unavoidable reasons the Co PI will present the proposal.

(6). Independent consultants/experts will be invited to offer their opinion on specific research proposals if needed.

(7). the decisions will be minute and Chairperson's approval taken in writing.

Table 1: Types of risk

Type of risk	Definition/description
Less than minimal	Probability of harm or discomfort is nil or not expected.
Minimal risk	Probability of harm or discomfort anticipated in the research is not greater than encountered in routine life activities/ serious harm or adverse event is unlikely
Minor increase over minimal risk or Low risk	Increment in probability of harm or discomfort is only a little more than the minimal risk threshold. Such research should have a social value. Social risks, psychological harm and discomfort may also fall in this category.
More than Minimal/high risk	Probability of harm or discomfort anticipated in the research is invasive and greater than minimal risk or interventional study.

1. Exemption from review

Proposals which present less than minimal risk fall under this category as may be seen in following situations:

(a). Research on educational practices such as instructional strategies or effectiveness of or the comparison among instructional techniques, curricula, or classroom

management methods.

Exceptions:

(a)When research on use of educational tests, survey or interview procedures, or observation of public behavior can identify the human participant directly or through identifiers, and the disclosure of information outside research could subject the participant to the risk of civil or criminal or financial liability or psychosocial harm.

(b). When interviews involve direct approach or access to private papers.

2. Expedited Review

The proposals presenting no more than minimal risk to research participants may be subjected to expedited review. The Member- Secretary and the Chairperson of the CREC or designated member of the Committee or Subcommittee of the CREC may do expedited review only if the protocols involve -

1. Minor deviations from originally approved research during the period of approval (usually of one year duration).
2. Revised proposal previously approved through full review by the CREC or continuing review of approved proposals where there is no additional risk or activity is limited to data analysis.
3. Research activities that involve only procedures listed in one or more of the following categories:

   (a). Clinical studies of drugs and medical devices only when -

   (i). research is on already approved drugs except when studying drug interaction or conducting trial on vulnerable population or

   (ii). Adverse Event (AE) or unexpected Adverse Drug Reaction (ADR) of minor nature is reported.

4. Research involving clinical materials (data, documents, records, or specimens) that have been collected for non-research (clinical) purposes.

5. When in emergency situations like serious outbreaks or disasters a full review of the research is not possible, prior written permission of CREC may be taken before use of the test intervention. Such research can only be approved for pilot study or preliminary

work to study the safety and efficacy of the intervention and **the same participants should not be included** in the clinical trial that may be initiated later based on the findings of the pilot study.

(a). Research on interventions in emergency situation

When proven prophylactic, diagnostic, and therapeutic methods do not exist or have been ineffective, physicians may use new intervention as investigational drug (IND) / devices/ vaccine to provide emergency medical care to their patients in life threatening conditions. Research in such instance of medical care could be allowed in patients -

(i). when consent of person/ patient/ responsible relative or custodian/ team of designated doctors for such an event is not possible. However, information about the intervention should be given to the relative/ legal guardian when available later;

(ii). When the intervention has undergone testing for safety prior to its use in emergency situations and sponsor has obtained prior approval of DCGI;

(iii). only if the local IEC reviews the protocol since institutional responsibility is of paramount importance in such instances.

(iv). If Data Safety Monitoring Board (DSMB) is constituted to review the data;

(b). Research on disaster management

A disaster is the sudden occurrence of a calamitous event at any time resulting in substantial material damage, affecting persons, society, community or state(s). It may be periodic, caused by both nature and humans and creates an imbalance between the capacity and resources of the society and the needs of the survivors or the people whose lives are threatened, over a given period of time. It may also be unethical sometimes not to do research in such circumstances. Disasters create vulnerable persons and groups in society, particularly so in disadvantaged communities, and therefore, the following points need to be considered when reviewing such research

(i).Research planned to be conducted after a disaster should be essential, culturally sensitive and specific in nature with possible application in future disaster situations.

(ii).Disaster-affected community participation before and during the research is essential and its representative or advocate must be identified.

(iii).Extra care must be taken to protect the privacy and confidentiality of participants and communities.

(iv).Protection must be ensured so that only minimal additional risk is imposed.

(v).The research undertaken should provide direct or indirect benefits to the participants, the disaster-affected community or future disaster- affected population and *a priori* agreement should be reached on this, whenever possible, between the community and the researcher.

(vi).All international collaborative research in the disaster-affected area should be done with a local partner on equal partnership basis.

(vii).Transfer of biological material, if any, should be as per Government rules taking care of intellectual property rights issues.

6. Expedited review may also be taken up in cases of nationally relevant proposals requiring urgent review.

Ethical Review Procedures

3. Full Review

All research presenting with more than minimal risk, proposals/ protocols which do not qualify for exempted or expedited review and projects that involve vulnerable population and special groups shall be subjected to full review by all the members.

While reviewing the proposals, the following situations may be carefully assessed against the existing facilities at the research site for risk/benefit analysis:

(a). Collection of blood samples by finger prick, heel prick, ear prick, or vein puncture:

(i). from healthy adults and non-pregnant women who weigh normal for their age and not more than 500 ml blood is drawn in an 8 week period and frequency of collection is not more than 2 times per week;

(ii). from other adults and children, where the age, weight, and health of the participants, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected has been considered and not more than 50 ml or 3 ml per kg, whichever is lesser is drawn in an 8 week period and not more than 2 times per week;

(iii).from neonates depending on the hemodynamic, body weight of the baby and other purposes not more than 10% of blood is drawn within 48 – 72 hours. If more

than this amount is to be drawn it becomes a risky condition requiring infusion/blood transfusion;
(iv). Prospective collection of biological specimens for research purposes by noninvasive means. For instance:
(1). Skin appendages like hair and nail clippings in a non-disfiguring manner;
(2). Dental procedures - deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction of permanent teeth; supra and sub-gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth;
(3). Excreta and external secretions (including sweat);
(4). Uncannulated saliva collected either in an unstipulated fashion or stimulated by chewing gum or by applying a dilute citric solution to the tongue;
(5). Placenta removed at delivery;
(6). Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
(7). Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
(8). Sputum collected after saline mist nebulization and bronchial ravages.

(b). Collection of data through noninvasive procedures routinely employed in clinical practice. Where medical devices are employed, they must be cleared/ approved for marketing, for instance
(i). physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the participant or an invasion of the participant's privacy;
(ii). Weighing or testing sensory acuity;
(iii).Magnetic resonance imaging;
(iv). Electrocardiography, echocardiography; electroencephalography, thermography, detection of naturally occurring radioactivity, Electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow,
(v). moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
(c). Research involving clinical materials (data, documents, records, or specimens) that will be collected solely for non-research (clinical) purposes.

(d). Collection of data from voice, video, digital, or image recordings made for research purposes.
(e). Research on individual or group characteristics or behavior not limited to research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies

XIV. Aspects considered during review of research proposal.

(1). Scientific design and conduct of the study.
(2). Approval by appropriate scientific review committees / Research committee.
(3). Examination of predictable risks/harms
(4). Examination of potential benefits.
(5). Procedure for selection of subjects including inclusion / exclusion, withdrawal criteria and other issues like advertisement details.
(6). Management of research related injuries, adverse events.
(7). Compensation provisions.
(8). Justification for placebo in control arm, if any
(9). Availability of products, benefits to subjects after the study is completed if applicable.
(10). Patient information sheet, informed consent form in English and in local languages.
(11). Protection of privacy and confidentiality.
(12). Involvement of the community, wherever necessary
(13). Plans for data analysis and reporting.
(14). Adherence to all regulatory requirements and applicable guidelines.
(15). Competence of investigators, research and supporting staff.
(16). Facilities and infrastructure of study sites.
(17). Criteria for withdrawal of patients, suspending or premature termination of the study in Netaji Subhas Medical College & Hospital, Amhara, Bihta, Patna (Bihar)

XV. Decision-making:

(1). Members will discuss the various issues before arriving at a

consensus decision. When consensus is not arrived at, the decision will be made by voting procedure.

(2). A member should withdraw from the meeting during the decision procedure concerning an application where a conflict of interest arises and this should be indicated to the chairperson prior to the review of the application and recorded in the minutes.

(3). Decision will be made only in meetings where quorum is complete.

(4). only member can make the decision. The expert consultants will only offer their opinions.

(5). Decision may be to approve, reject or revise the proposals. Specific suggestions for modifications and reasons for modifications and reasons for rejection will be given.

(6). in cases of conditional decisions, clear suggestions for revision and the procedure for having the application revised will be specified.

(7). Modified proposals will be reviewed by an expedited review through identified members.

(8). Procedures for appeal by the researchers will be clearly defined.

XVI. Communicating the decision

1. Decision of the meeting on the proposals will be communicated by the Member Secretary in writing to the PI / Research Scholar within 10 working days after the meeting at which the decision was taken in the specified format (Annexure-5). A certificate of approval will be sent to the applicant within 2 weeks (Annexure-6). All the approvals will be valid for one year or for the duration of the project whichever is less. Investigator has to get his or her project re-approved after one year if necessary.

2. The communication of the decision will include:

(a). Name and address of CREC.

(b). The date, place and time of decision.

(c). the name and designation of the applicant.

(d). Title of the research proposal reviewed.

(e). The clear identification of protocol no., version no., date, amendment no., date.

(f). Along with protocol, other documents reviewed- Clear description of these documents along with Version No. and Date.

(g). List of EC members who attended the meeting- clear description of their role, affiliation and gender.

(h). A clear statement of decision reached.

(i). any advice by the CREC to the applicant including the schedule / plan of ongoing review by the NSMCH-CREC.

(j). In case of conditional decision, any requirement by CREC, including suggestions for revision, and the procedure for having the application re-reviewed.

(k). In case of rejection of the proposal, reason(s) for the rejection will be clearly stated.

(l). Signature of the member secretary with date.

XVII. Following up procedures for approved proposals by PI / Sponsor

(1). CREC will review the progress of all the studies for which a positive decision has been reached from the time of decision till the termination of the research.

(2). Progress of all the research proposals will be followed at a regular interval of at least once a year. But in special situations, CREC will conduct the follow up review at shorter intervals basing on the need, nature and events of research project.

(3). Periodic status report of study should be submitted at prescribed intervals for review, along with information and documents as specified in Annexure-4A, 4B 4C & 7 based on the safety concerns and this prescribed interval should be specified in the Letter of Communication of Decision to the PI from the CREC.

(4). Final report should be submitted at the end of study.

(5). Following instances and events will require the follow-up review/ Renewed Approval:

(a). Any protocol amendment likely to affect rights, safety or

well-being of research subject of conduct of study.

(b). Serious or unexpected ADR related to study or product, action taken by Investigator, Sponsor and Regulatory Authority.

(c). any event or information that may affect the benefit/risk ratio of the study.

6. Protocol deviation, if any, should be informed with adequate justifications.

7. Any new information related to the study should be communicated.

8. Premature termination of study shall be notified with reasons along with summary of the data obtained so far.

9. Change of investigators/sites must be informed to the office of CREC.

10. Monitoring: Oversight mechanism will be in place to monitor the approved studies. Actual site visits can be made especially in the event of reporting of adverse events or violations of human rights and appropriate action will be taken when required and communicated to the applicant indicating modification/suspension/termination /continuation of the project. In case the IEC desires so, reports of monitoring done by the sponsor and the recommendations of the DSMB may also be sought.

11. Applicant must inform the time of completion of study and must send the result summary to CREC. CREC must receive a copy of final summary of study completed from the applicant.

XVIII. Responsibilities of Sponsor/Investigator. - Responsibilities of Sponsor

(i) The clinical trial Sponsor is responsible for implementing and maintaining quality assurance systems to ensure that the clinical trial is conducted and data generated, documented and reported in compliance with the protocol and Good Clinical Practice (GCP) Guidelines issued by the Central Drugs Standard Control Organization, Directorate General of Health Services, Government of India as well as with all applicable statutory provisions. Standard operating procedures should be documented to ensure compliance with GCP and applicable regulations.

(ii) Sponsors are required to submit a status report on the clinical trial to the Licensing Authority

at the prescribed periodicity.

(iii) In case of studies prematurely discontinued for any reason including lack of commercial interest in pursuing the new drug application, a summary report should be submitted within 3 months. The summary report should provide a brief description of the study, the number of patients exposed to the drug, dose and duration of exposure, details of adverse drug reactions (Annexure 7), if any, and the reason for discontinuation of the study or non-pursuit of the new drug application

(iv) Any report of serious adverse event of death occurring in clinical trial, after due analysis shall be forwarded by the sponsor to chairman of the ethics committee and chairman of the expert committee constituted by the licensing authority as defined under rule 21(b) under appendix XII of gazette notification dated 30th January 2013 with a copy of the report to the Licensing authority and the head of the Institution where the trial has been conducted within ten calendar days of occurrence of serious adverse event of death. The report of the serious adverse event other than death, after due analysis, shall be forwarded by the sponsor to the Licensing authority, Chairman of the Ethics Committee and the head of the Institution where the trial has been conducted within ten calendar days of occurrence of the serious adverse event. (See Annexure 7).

(V). IN case of injury or death occurring to the clinical trial subject, the sponsor (whether a pharmaceutical company or an Institution) or his representative, whosoever had obtained permission from the Licensing Authority for conduct of the clinical trial, shall make payment for medical management of the subject and also provide financial compensation for the clinical trial related injury or death in the manner as prescribed in Appendix XII of gazette notification dated 30th January 2013.

(VI) The sponsor (whether a pharmaceutical company or an institution) or his representative, whosoever had obtained permission from the Licensing Authority for conduct of the clinical trial, shall submit details of compensation provided or paid for clinical trial related injury or death, to the Licensing Authority within thirty days of the receipt of the order of the Licensing Authority.

Responsibilities of the Investigator(s).-

(1) The Investigator(s) shall be responsible for the conduct of the trial according to the protocol and the GCP Guidelines and also for compliance as per the undertaking given in Appendix VII of schedule Y. Standard operating procedures are required to be documented by the investigators for the tasks performed by them. During and following a subject's participation in a trial, the investigator should ensure that adequate medical care is provided to the participant for any adverse events. Investigator(s) shall report all serious and unexpected adverse events to the Licensing Authority defined under clause (B) of rule 21 (Schedule Y and Gazette notification 30th January 2013), the sponsor or his representative, whosoever had obtained permission from the licensing authority for conduct of the clinical trial, and the ethics committee that accorded approval to the study protocol, within twenty four hours of their occurrence. The report of the serious adverse event of death, after due analysis shall be forwarded by the investigator to Chairman of the ethics committee and Chairman of the Expert Committee constituted by the Licensing authority under Appendix XII with a copy of the report to the Licensing Authority and the head of the institution where the trial has been conducted within ten calendar days of occurrence of the serious adverse event of death. The report of the serious adverse event other than death, after due analysis shall be forwarded to the Licensing Authority, Chairman of the Ethics Committee and the Head of the Institution where the trial has been conducted within ten calendar days of occurrence of the serious adverse event.

(2) The investigator shall provide information to the clinical trial subject through informed consent process as provided in Appendix V of Schedule Y about the essential elements of the clinical trial and the subject's right to claim compensation in case of trial related injury or death. He shall also inform the subject or His/ Her nominee(s) of their rights to contact the sponsor or his representative whosoever had obtained permission from the Licensing Authority for conduct of the clinical trial for the purpose of making claims in the case of trial related injury or death**.**

XIX. Record keeping and archiving at the office of NSMCH-

11/2/2021 01.02.2021 1/2/2021 01/02/2021

Prepared by Reviewed by Approved by

CREC:

(1). All the documents and communications of CREC will be dated, filed and archived in a secure place.

(2). only persons, who are authorized by the Chairman of CREC will have the access to the various documents.

(3). All the documents related to research proposals will be archived for a minimum period of 3 years in the Institute, following the completion /termination of the study.

(4). No document (except agenda) will be retained by any CREC member.

(5). at the end of each meeting, every member must return the soft copy containing all the research proposals and documents to CREC office staff. They will archive one copy in CREC office and other copies will be destroyed after one year.

(6). Following documents will be filed and archived with proper label on the top of file for easy identification

(a). Constitution and composition of NSMCH- CREC

(b). Curriculum Vitae (CV) of all members of NSMCH- CREC with records of training in Human ethics if any.

(c). Standard Operating Procedures of NSMCH- CREC.

(d). Annual reports

(e). A record of all income and expenses of the CREC, including allowances and reimbursements made to the secretariat and CREC members;

(f). The published guidelines for submission established by the CREC.

(g). Copy of all study protocols with enclosed documents, progress reports, and SAEs.

(h). Agendas and Minutes of all CREC meetings duly signed by the Chairperson / Member secretary.

(i). Copy of all existing relevant national and international guidelines on ethics and laws along with amendments.

(j). Copy of all correspondence with members, Principal Investigators and other regulatory bodies.

(k). Record of all notification issued for premature termination of a study with a summary of the reasons;

(l). Final report of the approved projects, including microfilms, CDs and Video recordings.

XX. Updating NSMCH- CREC members:

(1). All relevant new guidelines should be brought to the attention of the members.

(2). The CREC members should be encouraged to keep abreast of all national and international developments in ethics through orientation courses on related topics by its own members or regular training organized by constituted body/ (is), so that they become aware of their role and responsibilities. For drug trial review it is preferable to train the CREC members in Good Clinical Practice. Any change in the regulatory requirements should be brought to their attention and they should be aware of local, social and cultural norms, as this is the important social control mechanism. This is needed for maintaining quality in ethical review.

XXI. Terms of reference:

Terms of reference will be maintained in the office of NSMCH- CREC. This includes

(A). Membership Requirements

(B). Terms of Appointment with reference to the duration of the term,

(C). the policy for removal, replacement, resignation procedure,

(D). Frequency of meetings, and

(E). Payment of processing fee to the CREC for review, honorarium/ consultancy to the Members/ Invited experts *etc.*

The SOPs will be updated periodically based on the changing requirements. The term of appointment of members could be extended for another term and a defined percentage of members could be changed on regular basis. Preferably, CREC would appoint persons trained in bioethics or persons conversant with ethical guidelines and laws of the country. Substitute member may be nominated if meetings have been continuously missed by a member due to illness or other unforeseen circumstances.

S. No.	• Members of CREC	• Definition/description

1.	• Chairperson/ • Vice Chairperson (optional) • Non-affiliated • Qualifications - • A well-respected person from any background with prior experience of having served/ serving in CREC	• Conduct CREC meetings and be accountable for independent • and efficient functioning of the committee • Ensure active participation of all members (particularly non-affiliated, non-medical/ non- technical) in all discussions and deliberations • Ratify minutes of the previous meetings • In case of anticipated absence of both Chairperson and Vice Chairperson at a planned meeting, the Chairperson should nominate a committee member as Acting Chairperson or the members present may elect an Acting Chairperson on the day of the meeting. The Acting Chairperson should be a non-affiliated person and will have all the powers of the Chairperson for that meeting. • Seek COI declaration from members and ensure quorum • And fair decision making. • Handle complaints against researchers,CREC members, conflict of interest issues and requests for use of CREC data, etc.

2.	- Member Secretary/ Alternate Member Secretary (optional) - Affiliated - - Qualifications - - Should be a staff member of - the institution - Should have knowledge and experience in clinical research and ethics, be motivated and have good communication skills - - • Should be able to devote adequate time to this activity which should be protected by the institution	- Organize an effective and efficient procedure for receiving, preparing, circulating and maintaining each proposal for review - Schedule CREC meetings, prepare the agenda and minutes - Organize CREC documentation, communication and - archiving - Ensure training of CREC secretariat and CREC members - Ensure SOPs are updated as and when required - Ensure adherence of CREC functioning to the SOPs - Prepare for and respond to audits and inspections - Ensure completeness of documentation at the time of - Receipt and timely inclusion in agenda for CREC review. - Assess the need for expedited review/ exemption from - Review or full review. - • Assess the need to obtain prior scientific review, invite independent consultant, patient or community representatives. - • Ensure quorum during the meeting and record discussions - And decisions.
3.	- Basic Medical Scientist(s)Affiliated/ non-affiliated Qualifications - - •Non-medical or medical person with qualifications in basic medical sciences - •In case of CREC reviewing clinical trials with drugs, the basic medical scientist should preferably be a pharmacologist	- •Scientific and ethical review with special emphasis on the intervention, benefit-risk analysis, research design, methodology and statistics, continuing review process, SAE, protocol deviation, progress and completion report - •For clinical trials, pharmacologist to review the drug - Safety and pharmacodynamics.

4.	- Clinician(s) - Affiliated/ non-affiliated Qualifications - - •Should be individual/s with recognized medical qualification, expertise and training	- •Scientific review of protocols including review of the intervention, benefit-risk analysis, research design, methodology, sample size, site of study and statistics - •Ongoing review of the protocol (SAE, protocol deviation - or violation, progress and completion report) - •Review medical care, facility and appropriateness of the principal investigator, provision for medical car, management and compensation. - •Thorough review of protocol, investigators brochure (if - Applicable) and all other protocol details and submitted documents.
5.	- Legal expert/s - Affiliated/ non-affiliated Qualifications - - •Should have a basic degree in Law from a recognized university, with experience - •Desirable: Training in medical - law.	- •Ethical review of the proposal, ICD along with translations, MoU, Clinical Trial Agreement (CTA), regulatory approval, insurance document, other site approvals, researcher's undertaking, protocol specific other permissions, such as, stem cell committee for stem cell research, HMSC for international collaboration, compliance with guidelines etc. - •Interpret and inform EC members about new regulations - if any
6.	- Social scientist/ philosopher/ ethicist/theologian - Affiliated/ non-affiliated - Qualifications - - •Should be an individual with social/ behavioral science/ philosophy/ religious qualification and training and/or expertise and be sensitive to local cultural and moral values. Can be from an NGO involved in health-related activities	- •Ethical review of the proposal, ICD along - With the translations. - •Assess impact on community involvement, socio–cultural context, religious or philosophical context, if any - •Serve as a patient/participant/ societal / community representative and bring in ethical and societal concerns.

7.	- Lay person(s) - Non-affiliated Qualifications - - •Literate person from the public or - community - •Has not pursued a medical science/ health- - related career in the last 5 years - •May be a representative of the community - from which the participants are to be drawn - •Is aware of the local language, cultural and - moral values of the community - •Desirable: involved in social and - community welfare activities	- Ethical review of the proposal ,ICD along - With translation(s). - Evaluate benefits and risks from the participant's perspective and opine whether benefits justify the risks. - Serve as a patient/participant/ community representative and bring in ethical and societal concerns. - Assess on societal aspects if any.

XXII **ADMINISTRATION AND MANAGEMENT**

A full time secretariat and space for keeping records is required for a well-functioning CREC. The members could be given a reasonable compensation for the time spared for reviewing the proposals. Reasonable fees can be charged to cover the expenses related to review and administrative processes for any third party (protocols submitted by researchers not employed by NSMCH) submission as described in section XI Point No 6. There should be provision for allocating reasonable amount of funds for smooth functioning of the CREC

XXIII **Conflict of Interest**

CREC shall ensure to implement procedures to declare and management conflict of interest (financial/non-financial) of researchers, CREC members, institution, and sponsor.

Stringent norms and caution should be followed in the consent process when done

For research purposes.

(1). for routine genetic diagnostic testing, written consent may or may not be needed as Per institutional policies; however, for any research it is required.

(2). Informed written consent is essential for procedures such as pre-symptomatic testing, Next generation sequencing (NGS), prenatal testing, genomic studies, carrier status etc..3 It needs to be emphasized that consent for screening or a subsequent confirmatory test Does not imply consent to any specific treatment or termination of the pregnancy or For research.

(3). If the research or testing involves a child, appropriate age-specific assent (verbal/oral/written) should be obtained along with parental consent. See section 6 for further Details.

(4). In addition to the general contents specified in section 5, the consent form for genetic Testing for research may have explanations/details on the following elements:

• The nature and complexity of information that would be generated;

• The nature and consequences of return of results and choice offered to the Participant whether to receive that information or not and incidental findings, if Any;

• Direct/indirect benefits and their implications including if there are no direct Benefits to the participants;

• How the data/samples will be stored, for how long, and procedures involved in Anonymisation, sharing, etc.

• Choice to opt out of testing/withdraw from research at any time;

• Whether the affected individual or the proband would like to share her/his genetic Information with family members who may benefit from it; and

• Issues related to ownership rights, IPR concerns, commercialization aspects, Benefit sharing.

(5). Group consent/community consent

• In case of population or community based studies, it may be noted that the genetic Research may generate information applicable to the community/populations From which the participants were drawn, and therefore, group consent

must be
Taken from the community head and/or the culturally appropriate authority.
• Even if group consent is taken, it will not be a replacement for individual consent
As individual consent is important. See section 5 for further details.
• Researchers should be aware of potential stigmatization of the entire group
And must explain ways to avoid the same during the conduct of research and
Publication of research results.

(6). culturally sensitive issues

(1). Transmission of a genetic abnormality from parents, especially the mother to the Fetus could be a very sensitive cultural issue. Such possibility arises when during Routine testing or prenatal diagnosis it is revealed that the wife is a carrier of X-linked Or recessive disease affecting the foetus or making it a carrier of fatal or late onset Disease conditions, such as hemophilia, Huntington's disease, non-syndrome deafness and mitochondrial conditions where a female foetus could transmit the abnormality to the next progeny, etc. If information is revealed to the husband or other members Of the family, it may cause marital discord despite the fact that the husband himself is A carrier of the autosomal recessive disorder. Appropriate counseling should be part Of the testing process.

(2). Consanguineous marriages are common in some communities. If there are inherited Diseases detected in the family, it is the responsibility of the health professionals/ Researchers to inform participants regarding the possible implications that may arise Due to consanguinity. Appropriate pedigrees need to be prepared and stored, as these Can reveal a lot regarding disease inheritance in affected families.

(7). Storage of samples for future genetic research

1. Rapid advance in science and technology have necessitated the storage of biological Materials for future genetic research.

2 The samples from patients with rare genetic conditions, ethnic

groups/tribes/
Populations on the verge of extinction, endogamous groups and others have great Cultural and geographical value and need to be preserved for future research. See Section 11 for further details.

(8). Results of genetic testing

(1). Results of the tests should be informed to the participants. Return of the results Depends on the research findings. If results are anticipated to be actionable, leading to Potential benefits of improving health outcomes through correction of diet as therapy or prevention (such as phenylketonuria) by delaying onset or reduction of disease Burden, they need to be communicated to the participants. This should also be reported To the participants if they wish to know the results and must be specified in the ICD. For this, participants' contact details should be available.

(2). the researcher should work with the local EC to decide on the validity of the research Finding and the severity of the potential disease in order to return the results which Should be avoided if the logical outcome of the research is expected to be inconclusive And the participants were informed of this in the ICD.

(3). Results cannot be returned for the advantage of participants when the research is done Using irreversibly anonymized samples or data, as identifying the individuals is not Possible.

(9). Publication aspects

(1). Publication of pictures, pedigrees or other identifying information about individuals, Families or secondary participant(s) should be done with fresh or re-consent.

(2) .Features on the face should be masked to prevent identification. If these features have To be revealed for scientific reasons, this fact should be stated clearly in the informed Consent form and fresh consent must be obtained, if not taken earlier.

(10). Commercialization and COI

(1). Direct to consumer testing (DTC) in laboratories offering a

battery of genetic tests
is rapidly growing. While this ensures a patient's autonomy to undergo testing, it is Important that the sensitivity and specificity of these investigations and the ability of The laboratory personnel to interpret the result in consultation with treating physician/ Clinical geneticist is ensured before arriving at a diagnosis.

(2). When research is conducted by commercial companies, steps should be taken to protect Researchers and participants from possible coercion or inducement.

(3). Academic or research institutions require a review to probe possible COI between Scientific responsibilities of researchers and business interests (for example ownership Or part-ownership of the researcher in the company developing a new product).

(4). An EC should determine if the COI could damage the scientific integrity of a proposal Or cause harm to research participants and should advise accordingly.

(5). Institutions need self-regulatory processes to monitor, prevent and resolve such COI And assess the need of informing prospective participants.

(11). ICMR National Ethical guidelines 2017 policies on handling and mitigation of COI in special circumstances like genetic testing and research, quality standards of the laboratory, misuse of genetic technology, genetic diagnosis/ testing screening, gene therapy, use of newer technologies, research on human embryo, foetal autopsy shall be followed, as and when required.

XXIV Informed Consent

The CREC will ensure that the participants have been given sufficient, accurate information about the study.

The Informed Consent document should contain all of the information that the participant Needs to make an informed decision about taking part in the study.

The participant must sign and date the informed consent document before taking part in any study procedures.

The consent form should be written in non-technical language that participants would understand. Also, it should be written in language consistent with the participants'

educational level, cultural views, and familiarity with research.

The participant may withdraw consent and decline to participate in the study at any time before or after signing the consent document until their participation in the study is completed.

The informed consent should state those aspects of the study/trial that are experimental, the risk and the benefits of the study/trial, the number of participants involved as well as the expected duration of the participant's involvement in the study/ trial.

CREC will ensure that adequate provision is made to protect subject's privacy and maintain the confidentiality of data. It should state the compensation and/or treatment available to the participant in the event of trial-related injury.

It should state the anticipated expenses, if any, to the participant for participating in the study and the anticipated prorated payment, if any, to the participant for participating in the study. (Also refer section XXV- 9, Informed Consent)

XXV Ethical Review Procedures for Emergency Review/ COVID-19

1. Categories of Research:

(1). There are 3 categories of research during COVID that may require ethics review.

□□ New research directly related to COVID-19

□ Ongoing non-COVID research

□ New non-COVID research

CREC shall prioritize research review based on urgency and take needful steps to facilitate the review of new research and conduct ongoing research with needful amendments as per need in the view of social distancing norms.

2. Role of CREC

(1).CREC shall ensure a thorough scientific and ethical review of research as per national guidelines and regulations to safeguard the dignity, rights, safety and well-being of research participants.

(2).CREC is to be registered with appropriate agencies – DHR for biomedical and health research and CDSCO for regulatory clinical trials as per New Drug and Clinical Trial Rules, 2019.

(3).CREC to ensure that all COVID-19 related research (all clinical trials as well as biomedical and health research) be registered on Clinical Trial Registry of India (CTRI) and seek approvals as per relevant guidelines and applicable regulations.

(4).Member Secretary to categories proposals into exempt/expedited/ or full review category as per National Ethical Guidelines and plan next steps for fast track review.

(5).Research during emergencies can be reviewed through expedited review/unscheduled full committee meetings on a case-to-case basis depending on the urgency and need. If an expedited review is done, full ethical review can follow whenever next possible.

(6).Quorum for decision-making should have a minimum of five members, including both medical/non-medical and technical/non-technical members with one non-affiliated member.

(7).**Measures such as virtual or tele/web conferences should be attempted and face-to-face meetings can be avoided to observe social distancing norms.**

(8).In exceptional and emergency situations, preliminary research procedures including but not restricted to data/ biological sample collection that are likely to rapidly deteriorate or perish may be allowed while the ethics review process is still underway.

(9).Available protocol templates could be reviewed to expedite the process and interim review/ re-review can be done if the emergency situation changes.

(10).CREC shall develop procedures to ensure timely review and monitoring of the approved research. On a case-by-case basis, may require re-review with time and circumstances.

Table 2: Ethical issues related to reviewing a protocol

Social values	Scientific design and conduct of study	Review of informed consent process
Benefit–risk assessment	Selection and recruitment of participants	Qualification & adequacy of study sites
Payment for participation	Disclosure of conflict of interest	Plans for medical management and compensation for study related injury
Community considerations	Protection of privacy and confidentiality	

Special Situations:

(1).As per ICMR guidelines on COVID-19, Institution (NSMCH) may utilize services of another institution with mutual agreement and agree to be overseen by it.

(2).Once registered, CREC can review protocols of researchers who have no institutional attachments or of institutions without their own ethics committees.

(1).NSMCH could have subcommittees such as SAE subcommittee or expedited review committee which report to the main CREC. These comprise Chairperson/ Member Secretary and one to two designated members of the main CREC as defined in the SOPs.

Ethics Review:

(1).Researchers should submit research proposals in the proposed format for Ethics Review as soft or hard copies (3) enclosing required documents.

(crecnsmch@gmail.com)

(2).Submission of e-copy of research protocol and relevant documents followed by their screening by Member secretary for completeness and categorization as exempt/ expedited review/ emergency full committee review depending on the urgency and need.

(3).Electronic documents may be accepted for review and timelines shortened for accelerated procedures.

(4).Virtual or Tele/Video conferences should be attempted to ensure social distancing as face-to face meetings may not be suitable. Use suitable virtual software platform, preferably a video conference to enable face to face discussion or teleconference if connectivity is an issue.

(5).Agenda of virtual meetings shall be kept short, however, CREC may meet more frequently for fast track review within in 24-48 hrs.

(6).CREC may plan a prior review by subject experts/obtain clarifications from researchers before the meeting or/ invite independent consultants (non-voting) or representative from specific patient group as special invitee. The special invitees invited for the web-meeting may be asked to leave the meeting before final decision making.

(7). During the review process, the CREC shall consider the following:

If written consent is not possible (e.g., physical isolation/severe COVID-19 patients), consent could be given orally/ use electronic methods to document and record.

Due to inability of the participant to attend the site (for e.g., social distancing), the contact/communication can be made via phone, to enquire and identify adverse events, serious adverse events and ensure medical care and oversight with documentation.

In an ongoing study, if the designated principal investigator (PI) is indisposed for a period, she/he may need delegate parts of her/his duties temporarily to others/ co-investigator and the same should be documented and reported to CREC at the earliest.

(8).Withholding information in Public Health emergencies may be a threat to national security, and therefore the right balance must be maintained to protect individual privacy and confidentiality, and relevant disclosure to public health authorities.

(9).Steps would be taken to protect participants of researchers from possible stigma or discrimination.

(10).CREC members present during the virtual meeting should decide through consensus or cast online vote expressing their decision. Any disagreement to be recorded with reasons.

(11). Meeting could be digitally recorded (audio/video) with permission of members and member secretary is responsible to note the attendance/ participation in the online meeting.

Review of Multicentre Research:

(1).Common review of multicentre research in India can be carried out by one main designated Ethics committee (EC) for fast track decision making.

(2).CREC is free to accept the decision of designated committee or to do an expedited or full committee review expeditiously. CREC shall ensure ethics review of local site specific issues or concerns, informed consent translations, local study implementation and monitoring.

(3).Common review is generally carried out for research involving low or minimal risk, survey or multicentric studies using anonymized samples or data or those that are public health research studies determined to have low or minimal risk.

(4).However, in an emergency situation like the current one, for all types of research including high risk studies or those involving vulnerable population can be taken up for fast track common review while ensuring strict monitoring and oversight by registered local ethics committees.

Continuing Review & Monitoring:

(1). CREC shall continually evaluate progress of ongoing proposals, monitor approved study site for compliance, review SAE reports, protocol deviations/violations/ non-compliance/ DSMB reports/ any new information/assess final reports.

(2). For protocol deviations/violations the CREC shall examine the corrective actions. If the violations are serious the CREC may halt the study.

(3). Compensation must be given for research-related injuries if applicable, as determined by the CREC and as per regulatory requirement (if applicable).

Decisions Regarding Ongoing Studies:

(1). The impact of COVID-19 on ongoing and existing studies, ongoing recruitment and continued involvement of participants needs to be considered.

(2). Member secretary in consultation with Chairperson must carefully evaluate need for other non COVID-19 research studies that are ongoing/ near term/ have direct benefit(s) and if stopped, may pose risk to participants. These may be continued/suggest mechanisms for continuation.

(3).Following measures can be taken in consideration such as, extension of study duration; temporary halt of study at some/all sites; Suspension/ Postponement of study or activation of sites that have not yet been initiated without compromising safety and well-being of patients; Continuation of study with limited parameters; conversion of physical visits into phone or video visits, postponement or complete cancellation of visits to ensure that only strictly necessary visits are performed at sites; ongoing study may need to take re-consent of already enrolled participants to implement urgent changes; it can be done via phone or video-calls and obtaining oral consents supplemented with email confirmation.

(4).Further, travel restrictions, confinement of study participants and staff to perform visits should

be taken into account.

Review of new non-COVID Research:

(1).If priority for ethics review in a defined timeframe is given to COVID-19 related research; non-COVID research must not suffer due to *'covidisation'*. Studies evaluating treatments for chronic conditions or other communicable diseases or injuries or others shall also be considered for review by CREC as these may also be important.

(2).CREC shall review and assess if a planned study may have a negative impact on participants' safety or increase risk to participants (as a result of the ongoing COVID-19 pandemic), and make (a).decision to allow or not allow it so. It may also make relevant suggestions for additional safeguards for conducting research in such emergency.

(c). The review of these studies may be done through virtual CREC meeting ensuring appropriate scientific and ethical review and fulfilling the quorum requirements.

Informed Consent

(1). Informed Consent Process:

(1).Obtaining valid informed consent in humanitarian emergencies such as COVID-19 is a challenge due to practical difficulties in reaching out to a patient, who may be in a COVID ward, isolation or quarantine facility. In addition, the decisional capacity of the hospitalized patient with moderate or critical disease condition would be very low and it may not be possible to differentiate between reliefs offered and research components.

(2).Informed consent is a continuous process involving three main components – providing relevant information, ensuring competence, ensuring comprehension and voluntariness.

Table 3: Elements of an ICD

Elements of an ICD	Additional elements (optional)
1. Statement mentioning that it is research	1. Alternative procedures or treatment
2. Purpose of research and methods	2. Insurance coverage
3. Duration, frequency, methods	3. Possible stigmatizing condition
4. Benefits to participant, community or others	4. Biological material and data, including
5. Foreseeable risks, discomfort or inconvenience	i. Current and future uses
6. Confidentiality of records	ii. Period of storage, secondary use, sharing
7. Payment/reimbursement for participation	iii. Right to prevent use of biological sample
8. Treatment and/or compensation for injury	iv. Provisions to safeguard confidentiality
9. Freedom to participate/withdraw	v. Post-research plan/benefit sharing
10. Identity of research team and contact persons	vi. Publication plan/photographs/pedigrees

(3).Needful procedure be followed as discussed in National ethical guidelines for involving children (assent) or legally authorized representative (LAR) in case a participant is incompetent (medically or legally), illiterate participant/LAR should be witnessed by an impartial literate witness.

(4).Broad consent with an individual informed opt-out option may be used for research on residual clinical samples.

(5).The Informed Consent Document (ICD) has two parts – patient/participant information sheet (PIS) and the informed consent form (ICF) and can be prepared preferably utilizing electronic formats or plan methods to obtain consent maintaining adequate social distancing.

2 Electronic Consent:

(1).In light of COVID-19 infection control measures, the alternative procedures to avoid direct interaction with the patient in isolation shall be explored.

(2).Technology shall be utilized to prepare interactive formats and using electronic tools such as text, graphics, audio, video, podcasts, interactive website, platforms to explain information related to a study and to electronically document informed assent/consent the same.

(3).Electronic methods (e.g. digital signature) shall be reviewed and approved by the CREC a priori.

(4).Process can be documented through audio or video recording (if required).

3 Waiver of Consent:

(1).For seeking waiver of consent, the researchers should give the

rationale justifying the waiver which CREC can approve a waiver after careful discussion in the following situations:

(a).research cannot practically be carried out without the waiver and the waiver is scientifically justified like, cluster randomization trials.

(b).retrospective studies, where the participants are de-identified or cannot be contacted

(c). research on anonymized biological samples/data

- certain types of public health studies/surveillance programs/program evaluation studies
- research on data available in the public domain; or

(d.)Research during humanitarian emergencies and disasters, when the participant may not be in a position to give consent.

(e).When consent of the participant/LAR/assent is not possible due to the emergency situation, informed consent can be administered at a later stage, when the situation allows for it, and if it is so envisaged, prior permission must be obtained from the EC.

XXVI. Vulnerability

(1). Vulnerable Persons is individuals/ belonging to certain groups of persons who are relatively or absolutely incapable of protecting their own interests such as:

(1). Research involving children, pregnant and lactating women, vulnerable participants and those with diminished autonomy besides issues pertaining to commercialization of research and international collaboration. The observations and suggestions of CREC will be given in writing in unambiguous terms in such instances. ICMR guidelines as applicable will be followed for protection of vulnerable population.

(2).COVID-19 patients may be additionally vulnerable of being stigmatized due to the contagious nature of the disease. Also at risk are health care workers in COVID-19 hospitals including doctors, nurses, ward staff, sanitation workers, security personnel, food suppliers, or others.

(3).Socially, economically or politically disadvantaged individuals such as the stranded migrant workers who are susceptible to being exploited; Incapable of making a

voluntary informed decision or whose autonomy is compromised temporarily or permanently;

(4). Able to give consent, but voluntariness/understanding compromised due to their situation;

(5). 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

(6).Terminally ill patients ready to consent in search of new interventions.

Only the full committee would do accord approval and perform initial and continuing review proposals involving vulnerable populations.

Principles of research among vulnerable populations

(1). Vulnerable population has an equal right to be included in research so that benefits occurring 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 group.

(3). Participants must be empowered, to the maximum extent possible, to enable them to decide by themselves whether or not to give assent/consent for participation.

(4). In vulnerable populations, 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 populations are to be included in research, all stakeholders must ensure those additional protections are in place to safeguard the dignity, rights, safety and wellbeing 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 benefit from the dependant's

participation, the feeling of being pressed to participate may be irresistible which will undermine the potential voluntariness of the consent to participate.

(1). Researchers must justify the inclusion of a vulnerable population in the research.

(2). CREC must satisfy itself with the justification provided and record the same in the proceedings of the CREC meeting.

(3). Additional safety measures should be strictly reviewed and approved by the ECs.

(4). The informed consent process should be well documented. Additional measures such as recording of assent and recon sent, when applicable, should be ensured.

(5)CREC shall also carefully determine the benefits and risks of the study and examine the risk minimization strategies.

(6). As potential participants are dependent on others, there should be no coercion, force, duress, undue influence, threat or misrepresentation or incentives for participation during the entire research period.

(7). Vulnerable persons may require repeated education/information about the research, benefits, risks and alternatives, if any.

(8). Research on sensitive issues such as mental health, sexual practices/preferences, HIV/ AIDS, substance abuse, etc. may present special risks to research participants.

(9). Researchers should be cognizant of the possibility of conflicting interests between the prospective participant and LAR and should be more careful.

(10). Participants may be prone to stigma or discrimination, specifically when the participant is enrolled as a normal control or is recruited from the general population in certain types of research.

(11). Efforts should be made to set up support systems to deal with associated medical and social problems.

(12). Protection of their privacy, confidentiality and rights is required at all times – during conduct of research and even after its completion.

(13). Whenever possible, ancillary care may be provided such as setting up of a facility, school for unattended children of the participants or a hospital, or counseling centre.

Obligations/duties of stakeholders

All stakeholders have different responsibilities to protect vulnerable participants. See Table 4 for further details.

Women in special situations

Women have equal rights to participate in research and should not be deprived arbitrarily of the opportunity to benefit from research. Informed consent process for some women can be challenging because of cultural reasons. Hence, the women may consider consulting their husbands or family members, if necessary. Although autonomy of the woman is important, the researcher must follow the requirements of local cultural practices so as not to disturb the harmony in the household/family/community.

(1). Participation of a woman in clinical trials or intervention studies that may expose her to risk is elaborated in Box …..

(2). Prenatal diagnostic studies – research related to prenatal diagnostic techniques in pregnant women should be limited to detecting foetal abnormalities or genetic disorders as per the Pre-Conception and Pre-Natal Diagnostic Techniques (Regulation and Prevention of Misuse) Act, 1994, amended in 2003 and not for sex determination of the foetus.

(3). Research on sensitive topics – when research is planned on sensitive topics, for instance, domestic violence, genetic disorders, rape, etc., confidentiality should be strictly maintained and privacy protected. In risk mitigation strategies, appropriate support systems such as counseling centers, police protection, etc. should be established. At no time should information acquired from a woman participant be unnecessary, hurtful or appear voyeuristic. The EC should be especially vigilant regarding these sensitive issues.

Table- 4 Obligations and Duties of the stakeholders

Stakeholders	Obligations / duties
Researchers	• Recognize the vulnerability of the participant and ensure additional safeguards are in place for their protection. • Justify inclusion/exclusion of vulnerable populations in the study. • COI issues must be addressed. • Have well defined procedures (SOPs) to ensure a balanced benefit-risk ratio. • Ensure that prospective participants are competent to give informed consent. • Take consent of the LAR when a prospective participant lacks the capacity to consent. • Respect dissent from the participant. • Seek permission of the appropriate authorities where relevant, such as for institutionalized individuals, tribal communities, etc. • Research should be conducted within the purview of existing relevant guidelines/regulations.
Ethics Committees	• During review, determine whether the prospective participants for a particular research are vulnerable. • Examine whether inclusion/exclusion of the vulnerable population is justified. • Ensure that COI do not increase harm or lessen benefits to the participants. • Carefully determine the benefits and risks to the participants and advise risk minimization strategies wherever possible. • Suggest additional safeguards, such as more frequent review and monitoring, including site visits. • Only the full committee should do initial and continuing review of such proposals. It is desirable to have empowered representatives from the specific populations during deliberations. • ECs have special responsibilities when research is conducted on participants who are suffering from mental illness and/or cognitive impairment. They should exercise caution and require researchers to justify cases for exceptions to the usual requirements of participation or essentiality of departure from the guidelines governing research. ECs should ensure that these exceptions are as minimal as possible and are clearly spelt out in the ICD. • ECs should have SOPs for handling proposals involving vulnerable populations.

Sponsors	• The sponsor, whether a government, an institution or a pharmaceutical company, should justify the inclusion of vulnerable groups in the protocol and make provisions for protecting their safety. • The sponsor must enable monitoring and ensure that procedures are in place for quality assurance (QA) and quality control (QC). • The sponsor should ensure protection of the participants and research team if the research is on sensitive topics.

Box 03 – Risks for women in Clinical trials/Interventions

1. Researchers must provide the EC with proper justification for inclusion of pregnant and nursing women in clinical trials designed to address the health needs of such women or their foetuses or nursing infants. Some examples of justifiable inclusion are trials designed to test the safety and efficacy of a drug for reducing perinatal transmission of HIV infection from mother to child, trial of a device for detecting foetal abnormalities or trials of therapies for conditions associated with or aggravated by pregnancy, such as nausea, vomiting, hypertension or diabetes.
2. If women in the reproductive age are to be recruited, they should be informed of the potential risk to the foetus if they become pregnant. They should be asked to use an effective contraceptive method and be told about the options available in case of failure of contraception.
3. A woman who becomes pregnant must not automatically be removed from the study when there is no evidence showing potential harm to the foetus. The matter should be carefully reviewed and she must be offered the option to withdraw or continue. In case the woman opts for continued participation, researchers and sponsors must adequately monitor and offer support to the woman for as long as necessary.

Children

Children are individuals who have not attained the legal age of consent (up to 18 years). At Younger ages, children are considered vulnerable because their autonomy is compromised As they do not have the cognitive ability to fully understand the minute details of the Study and make decisions. At older ages, although they may attain the cognitive ability to Understand the research; they still lack legal capacity to consent. Therefore, the decision Regarding participation and withdrawal of a child in research must be taken by the parents/ LAR in the best interests of their child/ward. More details are available in ICMR "National Ethical Guidelines for Bio-Medical Research involving Children, 2017".24

Research on children can be carried out in a situation, condition, disorder or diseases as Described in Box 6.4.

(1).The CREC shall do the benefit–risk assessment to determine whether there is a need to Put into place additional safeguards/protections for the conduct of research in children. For example, research should be conducted in child-friendly settings, in the presence of Parent and where child participants can obtain adequate medical and psychological Support.

(2).The CREC shall take into consideration the circumstances of the children to be enrolled In the study including their age, health status, and other factors and potential benefits To other children with the same disease or condition, or to society as a whole.

(3).Consent of the parent/LAR is required when research involves children. See Box … For further details.

(4). Assent In addition to consent from parents/LARs, verbal/oral or written assent, as approved By the CREC, should be obtained from children of 7–18 years of age. As children grow, their Mental faculties develop and they are able to understand and respond. Respecting the Child's reaction, the child is made a party to the consent process by the researcher, who explains the proposed research in a very simple manner, in a language that ensures, that The child understands the request to participate in the research. A child's agreement to Participate in research is called assent. If the child objects, this wish has to be respected.

At the same time, mere failure to object should not be construed as assent. However, if the test intervention is likely to be lifesaving and is available only if the child participates in the study, the dissent by the child may be disregarded provided parental consent and
Prior approval from the EC is obtained. Requirements of assent are given in Box……..

Content of the assent form has to be in accordance with the developmental level
And maturity of the children to be enrolled and explained while considering the
Differences in individual understanding. The language of the assent form must
Be consistent with the cognitive, social and emotional status of the child. It must
Be simple and appropriate to the age of the child. Points to be included in the
Assent form is as given below:
An explanation about the study and how it will help the child;
An explanation of what will be done in the study, including a description of any discomfort that the child is likely to feel;
The contact information of the person whom the child can approach if she/
He needs an explanation; and
A paragraph emphasizing that the child can refuse to participate in the
Study and if she/he chooses to do so, the treatment at the centre will not
Be compromised.
The above list is not exhaustive and may be dealt with on a case to case basis.
• Waiver of assent: All the conditions that are applicable to waiver of informed
Consent in adults also applies for waiver of assent in children. See section 5.7 for
Further details. If the available intervention is anticipated to definitely benefit the
Child but would be available only if the child participates in the study, waiver
Of assent could be allowed. However, this situation should be accepted only in
Exceptional cases where all forms of assent/consent have failed. In such cases,
Approval of the CREC shall be obtained.

Box 04: Conditions for research in children

Children can be included in research if the situation, condition, disorder or disease fulfils one of the following conditions:

1. It is exclusively seen in childhood.
2. Both adults as well as children are involved, but the issues involved are likely to be significantly different in both these populations.
3. Both adults as well as children are involved in a similar manner and are of similar nature in terms of morbidity, severity and/or mortality, wherever relevant, and studies in adults have demonstrated the required degree of safety and efficacy.
4. Test interventions are likely to be at least as advantageous to the individual child participant as any available alternative intervention.
5. Risk of test interventions that is not intended to benefit the individual child participant is low as compared to the importance of the knowledge expected to be gained (minor increase over minimal risk).
6. Research is generally permitted in children if safety has been established in the adult population or if the information likely to be generated cannot be obtained by other means.
7. The physiology of children is different from that of adults, and the pharmacokinetics of many drugs is age-dependent based on the maturation of the drug metabolism pathways. For example, children metabolize many drugs much more rapidly as compared to adults, hence the dose of the drug per kg of body weight that needs to be given, is much higher in children as compared to adults. The absorption of drugs also varies with age. Pharmacokinetics and toxicity profile varies with growth and maturation from infancy to adulthood.
8. The adverse effects of many drugs may also be different in children as compared to adults. For instance, tetracyclines cause teeth discoloration in young children, aspirin use is associated with Reye's syndrome in children.
9. Age appropriate delivery vehicles and formulations (e.g. syrups) are needed for accurate, safe, and palatable administration of medicines to infants and children.
10. The pathophysiology of many disorders is dependent on a child's growth, development and adaptive plasticity. Examples include adaptive changes in the motor system following a perinatal stroke.

Research involving sexual minorities and sex workers

There are unique challenges associated with research on sexual minorities and sex

Workers such as privacy, confidentiality, possibility of stigma, discrimination and Exploitation resulting in increased vulnerability.

(1). Protection of their dignity and provision of quality healthcare under these circumstances Should be well addressed in the research proposal, preferably in consultation with the Community before the proposal is finalized.

(2). It would be advisable to have a representative of the sexual minority group/ lesbian/ Gay/bisexual and transgender (LGBT) community as a special invitee/member to Participate in the meeting of the CREC if there is a research proposal involving these Participants.

(3).The CREC will suggest setting up of a community advisory board to act as an interface Between the researcher(s) and the community.

(4).Among the LGBT community there are inhibitions between the different groups, so Details of the research should be explained to each group separately.

(5).Peer educators or champions among the LGBT community could be educated and Sensitized first. They would in turn explain the details to the potential participants from The community who would then understand them better.

Research among tribal population

(1).Research on tribal populations should be conducted only if it is of a specific therapeutic, Diagnostic and preventive nature with appropriate benefits to the tribal population.

(2).Due approval from competent administrative authorities, like the tribal welfare Commissioner or district collector should be taken before entering tribal areas.

(3).Whenever possible, it is desirable to seek help of government functionaries/local bodies Or registered NGOs who work closely with the tribal groups and have their confidence.

(4).Where a panchayat system does not exist, the tribal leader, other culturally appropriate Authority or the person socially acceptable to the community may serve as the gatekeeper From whom permission to enter and interact should be sought.

(5).Informed consent should be taken in consultation with community elders and persons Who know the local language/dialect of the tribal population and in the presence of? Appropriate witnesses.

(6).Even with permission of the gatekeeper, consent from the

individual participant must

Be sought.

(7).Additional precautions should be taken to avoid inclusion of children, pregnant women And elderly people belonging to particularly vulnerable tribal groups (PVTG).25

(8).Benefit sharing with the tribal group should be ensured for any research done using Tribal knowledge that may have potential for commercialization.

(9).Research involving individuals with mental illness or cognitively impaired/affected Individuals

Mental illness: According to the World Health Organization, mental disorders comprise a broad range of problems, with different symptoms. They are generally characterized by some combination of abnormal thoughts, emotions, behavior and relationships

With others. According to the Mental Healthcare Act, 2017, 26 “mental illness” means a substantial disorder of thinking, mood, perception, orientation or memory that Grossly impairs judgment, behavior, and capacity to recognize reality or ability to meet The ordinary demands of life, mental conditions associated with the abuse of alcohol And drugs, but does not include mental retardation which is a condition of arrested or Incomplete development of the mind of a person, specially characterized by sub normality Of intelligence. Presence of a mental disorder is not synonymous with incapacity of Understanding or inability to provide informed consent.

Cognitively affected or impaired: Conscious mental activities such as thinking, Understanding, learning and remembering are defined as cognition. Those in whom these Activities are not fully functional are regarded as cognitively impaired. Such individuals Or groups include people who are without full intellectual potential (intellectually Disabled, previously called mentally retarded), unconscious, suffering from a number Of neuropsychological disorders such as dementia or delirium, and those who cannot Fully comprehend or participate in the informed consent process, either temporarily or Permanently. Other sources or reasons for cognitive impairment affecting the ability to Give informed consent include, but are not limited to, being too young (children do not Yet develop the necessary cognitive abilities to give informed consent); being in extreme Pain; being under the influence of medication, illicit drugs or

alcohol; mental retardation;

And traumatic brain injury (that causes unconsciousness or cognitive impairment while Conscious).

(10) .There is some psychiatric conditions that may lead people to cause risk or harm to Themselves or others.

• During the informed consent process, prospective participants must be informed About how the researcher will address a participant's suicidal ideation or other Risks of harm to themselves or others.

• It should be disclosed to the participant that her/his confidentiality may be Breached for reporting to family members, police, or other authorities or they may Have to be admitted in the hospital upon expression of such thoughts of harm to Self or others.

• While some interventions, like hospitalization and treatment for suicidality/ Homicidal ideas, may be primarily for the participants' own benefit, they Themselves may not perceive these as such and may want to refuse to participate in a study if any such interventions are required.

• Interventions should be of short duration, as least restrictive as possible and Invoked only when necessary, in accordance with relevant laws.

• Some research designs may reduce or violate human participant protections/rights Or specific requirements of informed consent by resorting to deception in order To achieve the objectives of the research for public good. Types of deception that Can be used in a research plan are described in Box 9.5. All such studies should be reviewed by the CREC very carefully before approval.

(11). Individuals who have diminished autonomy due to dependency or being under a Hierarchical system

While reviewing protocols that include students, employees, subordinates, defense Services personnel, healthcare workers, institutionalized individuals, under trials, Prisoners and others the CREC must ensure the following:

(1). Enrolling participants as described above is specifically pertinent to the research Questions and is not merely a matter of convenience.

(2). Individuals in a hierarchical position may not be in a position to disagree to participate For fear of authority and therefore extra efforts are required to respect their autonomy.

(3). It is possible for the participant to deny consent and/or later withdraw from the study Without any negative repercussions on her/his care.

(4). Mechanisms to avoid coercion due to being part of an institution or hierarchy should Be described in the protocol.

See Section 5 for informed consent issues.

(12). Patients who are terminally ill

Terminally ill patients or patients who are in search of new interventions having Exhausted all available therapies are vulnerable as they are ready to give consent for Any intervention that can give them a ray of hope. These studies are approved so that The scientific community or professional groups do not deny such patients the possible Benefit of any new intervention that is not yet validated.

(1). since therapeutic misconception is high there should be appropriate consent procedures And the CREC shall carefully review such protocols and recruitment procedures.

(2). Additional monitoring should be done to detect any adverse event at the earliest.

(3). Benefit-risk assessment should be performed considering perception of benefits and Risks by the potential participant.

(4).The CREC shall carefully review post-trial access to the medication, especially if it is Beneficial to the participant.

(13). other vulnerable groups

Other vulnerable groups include the economically and socially disadvantaged, homeless, Refugees, migrants, persons or populations in conflict zones, riot areas or disaster Situations. Additional precautions should be taken to avoid exploitation/retaliation/ Reward/credits and other inducements when such individuals are to be recruited as Research participants.

(1). Autonomy of such individuals is already compromised and researchers have to justify Their inclusion.

(2). CREC has to satisfy them with the justification provided to include these participants And record the same in the proceedings of the EC meeting.

(3). Additional safety measures suggested earlier in the guidelines should be strictly followed By the CREC.

(4). the informed consent process should be well documented. There should not be any Undue coercion or incentive for participation. A person's refusal to participate should Be respected and there should be no penalization.

(5). The CREC shall also carefully determine the benefits and risks of the study and examine Risk minimization strategies.

(14).Additional Safeguards: Participants may be under stress and traumatized, therefore, additional safeguards are required for participants and it should be ensured that,

(1). Research to address the needs of participants and justify inclusion of vulnerable persons.

(2). Benefits and risks carefully determined and the risk minimization strategies are examined.

(3). There is no coercion, force, undue influence, threat or misrepresentation or incentives.

(4). Informed consent processes is conducted in a respectful manner.

(5). Efforts to set up support systems to deal with associated medical and social problems.

(6). Protection of their privacy, confidentiality and rights is required at all times.

(7). Whenever possible, ancillary care may be provided.

Safety of Health Care Workers (HCW) involved in research:

(1). in wake of the pandemic, safety of researchers must get due attention as transmission of infection to one member in a lab or clinical setting could jeopardize the entire program.

(2). Ensuring safeties is the responsibility of the institution, sponsors and local authorities, since research team may be subjected to disturbing instances (trauma, humiliation and threats of violence) while conducting research.

(3). Additional precautions such as; Prioritize research and schedules to prevent overcrowding, adequate training, appropriate biosafety precautions, expose minimum number of researchers, communication using electronic platforms, due protection gear/PPE and facilities to undertake research, safety against any assault from public or others, insurance cover etc.

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