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Standard Operating Procedures (SOP) for the Review Committee for Protection of Research Rights to Humans (RCPRRH) of Indian Statistical Institute (ISI).

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Contents

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This SOP is accepted by the Director, Indian Statistical Institute for implementation on 21st June 2022.

1. Objective

The objective of this SOP is to put in place an effective and consistent ethical review mechanism for biomedical, social and behavioural science research for health involving human participants for all proposals submitted by the scientific workers and students of ISI as prescribed by the Ethical guidelines for NATIONAL ETHICAL GUIDELINES FOR BIOMEDICAL AND HEALTH RESEARCH INVOLVING HUMAN PARTICIPANTS of ICMR (2017).

2. Scope

These guidelines are applicable to all biomedical, social and behavioural science research for health conducted in India involving human participants, their biological material and data.

The purpose of such research should be:

- directed towards enhancing knowledge about the human condition while maintaining sensitivity to the Indian cultural, social and natural environment;
- conducted under conditions such that no person or persons become mere means for the betterment of others and that human beings who are participating in any biomedical and/or health research or scientific experimentation are dealt with in a manner conducive to and consistent with their dignity and well-being, under conditions of professional fair treatment and transparency; and
- subjected to a regime of evaluation at all stages of the research, such as design, conduct and reporting of the results thereof.

3. The Terms of Reference of the Committee

The Indian Statistical Institute Review Committee for Protection of Research Rights to Humans (ISI-RCPRRH) will review and approve all types of research proposals involving human participants with a view to safeguard the dignity, rights, safety and well-being of all actual and potential research participants. The goals of research, however important, should never be permitted to override the health and well-being of the subjects/participants. The ISI-RCPRRH will take care of all the

fundamental principles of research ethics namely, Respect for persons (autonomy), Beneficence, Non - malfeasance and Justice in planning, conduct and reporting of the proposed research for protecting the dignity, rights, safety and well-being of research participants. For this purpose, it will look into the aspects of informed consent process, benefit-risk assessment, privacy and confidentiality, distribution of burden and benefit, community engagement, selection of vulnerable and special groups as research participants, conflict of interest, and provisions for appropriate compensations, ancillary care wherever required. It will review the proposals before start of the study as well as monitor the research throughout the study until and after completion of the study through appropriate well documented procedures, such as annual reports, final reports and site visits etc. The committee will also examine compliance with all regulatory requirements, applicable guidelines and laws. The mandate of the ISI-RCPRRH will be to review all research projects involving human subjects including human biological materials and human biological data to be conducted at the Institute, irrespective of the funding agency.

4. Composition of ISI-RCPRRH

ISI-RCPRRH should be multi-disciplinary and multi-sectorial in composition. There should be adequate representation of age and gender. Independence and competence are the two hallmarks of an Institutional Ethics Committee. The number of persons in ISI-RCPRRH will be between 7-15 members. The Chairperson of the Committee should be from outside the Institute with prior experience of having served/ serving in an EC. The Member-Secretary/Convener will be a faculty member from the Institute to conduct the business of the Committee. Other members will be a mix of medical/nonmedical, scientific and non-scientific persons including lay public to reflect different viewpoints.

The composition committee should have the following members:

1. Chairperson (Not affiliated to the Institute) : 1
2. Basic Medical Scientist(s) (Affiliated to the Institute) : 1-3
3. Clinician(s) (Affiliated or not affiliated to the Institute) : 1-2
4. Legal expert(s) (Affiliated or not affiliated to the Institute) : 1-2

5. Social scientist/ philosopher/ ethicist/theologian (Affiliated or not affiliated to the Institute) : 1-3
6. Lay person(s), (Not affiliated to the Institute) : 1-2
7. Member-Secretary/Convener (Affiliated to the Institute) : 1

Special Invitee/ subject expert as independent consultants

As appropriate, the Committee will decide the need for participation of special invitees/ subject expert as independent consultants to have unbiased scientific and / or ethical opinion for the study protocol to be discussed. These special invitee may be specialists in ethical or legal aspects, specific diseases or methodologies, or represent specific communities; patient groups or special interest groups for opinion on a specific proposal, for example HIV, genetic disorders, or cancer, with appropriate decision making power. Special invitees shall participate in the discussion and deliberations but will not vote on a research proposal. However, the opinion of the special invitee shall be recorded.

5. Authority under which ISI-RCPRRH is constituted

Indian Statistical Institute RCPRRH (ISI-RCPRRH) is an Institutional standing ethics committee which functions independently. The Director, ISI will appoint the Chairperson and the Member-secretary/Convener based on their qualifications, competence and experience in reviewing and evaluating the scientific and ethical aspects of biomedical research proposals. Director in consultation with the Chairperson and the Member-secretary/Convener will appoint all other committee members, based on their qualifications, competence and experience in reviewing and evaluating the scientific and ethical aspects of biomedical research proposals.

6. Membership

Criteria for selection of members:

- Members are selected in their personal capacities, based on their interest, commitment and availability, ethical and/or scientific knowledge and expertise, experience in the domain field and profile.

- Conflict of interest will be avoided while making appointments, but where unavoidable, there will be transparency with regard to such interests.
- All members should maintain absolute confidentiality of all discussions during the meeting (Annexure: 01).
- Conflict of interest should be declared by members of the ISI-RCPRRH (Annexure: 02).
- The tenure/period of ISI-RCPRRH members will be for 3 years or till further orders.
- Director will not serve as member or ex-officio member.

7. Qualifications, roles and responsibilities of the members of ISI-RCPRRH

	Members of EC	Roles and responsibilities
1	Chairperson Qualifications – A well-respected person from any background with prior experience of having served/ serving in an EC	• Conduct EC 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, EC members, conflict of interest issues and requests for

		use of EC data, etc.
2	Member-Secretary/Convener 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 EC meetings, prepare the agenda and minutes • Organize EC documentation, communication and archiving • Ensure training of EC secretariat and EC members • Ensure SOPs are updated as and when required • Ensure adherence of EC 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 EC review. • Assess the need for expedited review/ exemption from review or full review
3	Basic Medical Scientist(s) Qualifications – • Non-medical or medical person	• 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
4	Clinician(s) 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 Qualifications – • Should have a basic degree in Law from a recognized university, with experience	• Ethical review of the proposal, ICD along with translations, MoU, regulatory approval, insurance document, other site approvals, researcher's undertaking, protocol specific other permissions, such as, stem cell committee for stem cell research, Health Ministry's Screening Committee (HMSC) for international collaboration, compliance with guidelines etc. • Interpret and inform EC members about new regulations if any
6	Social scientist/ philosopher/ ethicist/theologian Qualifications – Should be an individual with social/ behavioural science/ philosophy/ religious qualification and training and/or expertise and be sensitive to local cultural and moral values.	• 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) 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	• 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.

	values of the community • Desirable: involved in social and community welfare activities	

8. Quorum requirements for ISI-RCPRRH meetings

A minimum of five members including the Chairperson and member-secretary/Convener are required to compose a quorum. This quorum must include medical, non-medical or technical and/or non-technical members. Preferably the lay person should be part of the quorum. No decision of the committee will be valid without fulfillment of the quorum.

9. Procedure for resignation, replacement or removal of members

(a) Resignation

- A member can resign by submitting a letter of resignation addressed to the Chairman and delivered to the Member Secretary/Convener. The same will be informed by the Secretary to the appointing authority for formal acceptance (if approved) and to initiate necessary replacement/recruitment procedure for filling up the vacancy.
- The members if opts to step down due to any genuine cause may do so with prior notice of one month and proper information to the appointing authority.

(b) Replacement

- In case of resignation, the Director, ISI would appoint a new member, falling in the same category of membership e.g. legal expert with Legal expert.
- In case of superannuation of any member affiliated to the Institute, the Director, ISI would appoint a new member, falling in the same category of membership.
- Recommendations may be sought from the resigning member.
- Appointments may be made in consultation with the Member Secretary/ Convener and /or Chairperson.

(c) Disqualification

- If Director, ISI, Chairman or member secretary/Convener received a communication in writing alleging misconduct by a member subject to verification of the allegation by the appropriate authority.
- A member can be disqualified if fails to attend more than 3 regular consecutive ISI-RCPRRH meetings without prior intimation.
- If the member refuses to sign approval/disapproval to the minutes of the meeting after two reminders

10. Policy for updating/training of ISI-RCPRRH members:

- All relevant information on ethics will be brought to the attention of the members of ISI-RCPRRH by the Member Secretary/Convener.
- The Chairman, Member Secretary and members will be encouraged by the appointing authority to attend national and international training programs/conferences/workshops/seminars/courses at least once a year in the field of research ethics (over and above his own discipline) to help in improving the quality of review of research protocols/ethics committee submissions and other related activities.

11. Offices

The Chairperson will conduct all meetings of the ISI-RCPRRH. If for reasons beyond control, the Chairperson is not available, the Chairperson may appoint a chairperson among the members to conduct the meeting. The Member Secretary/Convener 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. Coordinator/Office assistant of the ISI-RCPRRH will communicate the decision to the researchers with the approval of the appropriate authority. Coordinator/Office assistant of the ISI-RCPRRH should maintain absolute confidentiality (Annexure: 03).

A list of members of the ISI-RCPRRH, bio-data and confidentiality agreement (Annexure: 01) would be maintained by Member Secretary/Convener of the ISI-RCPRRH.

This list and the copy of the working procedures would be made available to any investigator, for the purpose of filing of research projects, upon written request for the same to the Chairperson or Member-secretary/Convener.

12. Procedure for submission of research project for review by ISI-RCPRRH

- The Project Investigator has to submit the application to the Member Secretary/Convener of the ISI-RCPRRH in a prescribed format along with study protocol and other study related documents necessary for review of the ISI-RCPRRH (Annexure: 04).
- Application can be submitted to the office of the ISI-RCPRRH on any working day.
- All the proposals and documents must be submitted at least three weeks in advance by email to the ISI-RCPRRH (ethics@isical.ac.in) from the scheduled date of ISI-RCPRRH meeting.
- Soft copies of study proposal along with a cover letter and Informed consent form (English and local languages) and Consent form (English and local languages) must be submitted for ISI-RCPRRH review along with application form duly signed and dated by the investigator(s) to ethics@isical.ac.in
- Receipt of the application will be acknowledged by the ISI-RCPRRH office.
- Every application will be allotted an ISI-RCPRRH registration number to be used for all future correspondence and reference.

The application would include the following:

- Name, Designation and contact details of Principal Investigator. If the applicant is Research Associate, Post-doctoral fellow, Research scholar or students, the name, Designation and contact details of their supervisor should also be additionally mentioned.

- Title of the project and Name and contact details of Sponsor
- Research Objectives, Study Design, Materials and Methods of Data and Sample Collection. Clear research objectives and rationale for undertaking the investigation in human subjects in the light of existing knowledge.
- Subject recruitment procedures or proposed methods / advertisement / notices
- Inclusion and exclusion criteria for entry of subjects in the study.
- Precise description of methodology of the proposed research, including details of invasive procedures if any.
- The details of statistical analysis of the study.
- Procedure for seeking and obtaining informed consent with sample of patient information sheet and informed consent forms in English and the local language(s). Translation and back translation certificates (if applicable).
- Safety of proposed intervention (if any) including results of relevant laboratory and animal research.
- For research carrying more than minimal risk, an account of plans to provide medical therapy for such risk or injury or toxicity should be included.
- Case Record Form / Proforma / Questionnaire
- Proposed compensation for participation and reimbursement of incidental expenses/ serious adverse events occurring during the study participation.
- Plans for storage and maintenance of all data collected during the study period.
- Plans for publication of results, while maintaining the privacy and confidentiality of the study participants.
- A statement on probable ethical issues and steps taken to tackle the same.
- Activity plan / Timeline.
- Amendments to protocol (if any)
- Signature by the Principal investigator. If the applicant is Research Associate, Post-doctoral fellow, Research scholar or students, additional signature of the supervisor.

- All other relevant documents related to the study protocol including regulatory clearances and insurance documents as applicable.
- Details of Funding agency / Sponsors and fund allocation for the proposed work.
- Insurance policy of the study (if applicable).
- Undertaking by the Investigator
- Memorandum of Understanding (MOU) between collaborative institutions (if applicable)
- Ethics Committee clearance of other centers (if applicable)
- Recent curriculum vitae of the investigators indicating qualification and experience.
- Any additional document(s), as required by ISI-RCPRRH.

13. Procedure for initial scrutiny of proposals

- Every proposal will be collected and compiled by the ISI-RCPRRH office.
- An office staff/ member nominated by the Member Secretary/Convener/Director will verify the proposals for completeness.
- In case of incomplete data, the investigators will be informed by the office after consulting the Member-Secretary/Convener to make the necessary corrections and to resubmit.

14. Procedure for convening and conducting ISI-RCPRRH meetings

- Meetings will be planned in accordance with the need of the workload (but at least twice a year) & the Member Secretary/Convener in consultation with chairman may convene the ISI-RCPRRH meeting
- All the ISI-RCPRRH meetings will be held regularly on scheduled dates that are announced and notified in advance.
- All the proposals will be received at least three weeks before the meeting, checked for completeness as per the check list initially by the office assistant, subsequently by the member secretary/Convener.

- Members will be given not less than 10 days' time in advance to review study proposals and the relevant documents.
- Minutes of the ISI-RCPRRH meetings, all the proceedings and deliberation will be documented.
- Signatures of the Chairman, the Member Secretary/Convener & members will be obtained on the minutes of the meeting.
- Applicant or investigator may be invited to present the proposal or elaborate on specific issues.
- Independent experts may be invited to the meeting or to provide written comment, subject to applicable confidentiality agreement (Annexure: 01). They will not have a role in decision making of the ISI-RCPRRH.

15. Procedure for reviewing the research proposals

- Every proposal will be sent not less than 10 days before the meeting to all members of ISI-RCPRRH. They will evaluate them on ethical issues, scientific content, and technical excellence of the proposed research before it is taken up for ISI-RCPRRH review meeting.
- All the members will evaluate the possible risks to the study participants with proper justifications, the expected benefit and adequacy of documentation for ensuring privacy, confidentiality, and justice issue.
- Generally, the ISI-RCPRRH review will be done through formal meetings but if required ISI-RCPRRH can also decide through electronic circulation of proposal.
- Expert opinion of additional members would be obtained if necessary. Every proposal will be collected and compiled by the ISI-RCPRRH office.

16. Procedure for expedited review of research project by ISI-RCPRRH Sub-Committee

ISI-RCPRRH will receive and consider the proposals for expedited review and approval for the studies having/involving:

- No or minimum risk to the study participants.
- Re-examination of a proposal already examined by the ISI-RCPRRH.
- Study based only on secondary data involving no fieldwork.
- Similar study proposal for which ISI-RCPRRH had already given approvals earlier.
- When urgent studies are required.
- All proposal submitted by the PhD students, research associates and post-doctoral fellow of the Institute.
- All expedited approvals will be given in a meeting of the Sub-Committee of three members including the member secretary/Convener (nominated by the Chairperson). All three members including the Member Secretary/Convener should be present in the meeting.
- Decision taken by the Sub-Committee on expedited approval will be brought to the notice of the main committee members at the next regular meeting of the ISI-RCPRRH.

After review of the above mentioned study proposals, the ISI-RCPRRH sub-committee, if feels, may send it for Regular ISI-RCPRRH meeting with their recommendations.

All other proposals which do not comply with the above criteria will be reviewed in the Regular ISI-RCPRRH meeting.

17. Procedure for decision making regarding the research project

In making decision on application for the ethical review of any research proposal, ISI-RCPRRH will consider the following:

- Member having a conflict of interest will inform the Chairperson prior to the review of application and same will be recorded in the minutes.
- Where there is a conflict of interest, member will withdraw from the decision-making procedure.

- A decision will only be taken when sufficient time has been allowed for the review and discussion of an application in the absence of non-members (e.g. Investigator) from the meeting.
- Decision will only be taken at meetings where a quorum is complete.
- Decision will be taken only after reviewing a complete application with all the required documents necessary for proposal.
- Only ISI-RCPRRH members who participated in review and discussion will participate in decision making.
- Wherever possible, the decision will be arrived through consensus and not by vote, but when a consensus appears unlikely voting (> 66% of the members) can be resorted to.
- Decision will specify the conditional decision if any, with clear suggestions and re-review procedure.
- Rejection of proposal will be supported by clearly stated reasons.

Elements of Review

The submitted proposal shall be reviewed both for scientific content and ethical principles. The Committee members shall review the proposal with reference to the following:

- Scientific design of the study
- Justification / Rational of the study
- Selection criteria for subjects (Inclusion, exclusion criteria)
- Potential benefits to the study subjects, predictable risks to the study subjects
- Criteria for discontinuation / withdrawal of the subjects
- Monitoring of serious adverse events
- Compensation to the subjects for participating in the study
- Subject recruitment procedures (if applicable)
- Patient retention activities
- Compensation for study related injury or death
- Protection of privacy and confidentiality and plans for publication of results
- Methodology and Statistical analysis

- Informed consent document in English and regional languages
- Competence of the Investigators, supporting staff and infrastructure facilities
- Ethics Committee clearance of other centers (if applicable)
- Approval of regulatory authorities wherever applicable.

Criteria for the Approval of Research

In order to approve the research proposal, the Committee shall determine that all of the following requirements are satisfied:

- Risks to subjects, if any, are reasonable in relation to anticipated benefits. In evaluating risks and benefits, the Committee should consider only those risks and benefits that may result from the research.
- Selection of subject is equitable. In making this assessment, the Committee should take into account the purposes of the research and the setting, in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.
- Informed consent will be sought from each prospective subject or the Legally Authorized Representative of the subject.
- When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- In case, in which the documentation requirement is waived, the Committee may require the Investigator to provide subjects with a written statement regarding the research.
- When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

- Ethics Committee clearance of other centers/institutes of clinical collaborators of the investigator(s) (if applicable)
- The Committee shall have the authority to suspend or terminate approval of research that is not being conducted in accordance with the Committee's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reason(s) for the Committee's action and shall be reported promptly to the Investigator, appropriate institutional officials, Director and the funding agency (if applicable).

Safety Information

Adverse Event/ Serious Adverse Event reporting may be required for the protection of the subject

Types of decision:

- Approved: The study is approved in its present form. When committee approves the study, the certificate will be issued within a period of 15 days.
- Approved with modifications: This is a conditional approval. The revisions are required. If revisions are submitted within 6 months from the date of decision communicated to the PI and are found satisfactory, approval will be granted. If revisions are not submitted within 6 months from the date of decision communicated to the PI, the proposal will be considered as rejected.
- Resubmit: Extensive revisions are necessary. Principal Investigator has to comply with the changes suggested by ISI-RCPRRH during the meeting. The revised project will then be reviewed in the next meeting.
- Not approved: The study is not approved in its current form. The required modifications will be suggested during the meeting with reasons. If the investigator wishes to appeal to the decision, he/she may do so by contacting the ISI-RCPRRH Secretariat. The ISI-RCPRRH may decide to accept or deny the appeal. If the appeal is denied, the ISI-RCPRRH decision is final, and the study may not be approved or resumed.

- Defer: The decision cannot be arrived at present and therefore postpone to next meeting. Grounds for this: lack of quorum, lack of expertise etc.
- Maximum three deferment will be allowed.

Preparing and recording the minutes:

- The member-secretary/Convener will record the minutes of the meeting and disseminate the same to the members within a week of the meeting for their signed approval.
- The minutes of the ISI-RCPRRH meeting will be ratified in the subsequent ISI-RCPRRH meeting.
- In the record section of ISI-RCPRRH secretariat, approved minutes will be maintained by the coordinating staff with confidentiality (Annexure: 03) for a minimum period of five years both as soft and hard copies.
- The records will be maintained in such a way that it can be retrieved by tracking the records maintained in the tracking records of the minutes of the meeting.

Notification of Review Outcome

The outcome of the Committee review will be recorded and conveyed to the Investigator within 15 days from the date review.

Approval Period

All projects will be given approval for the duration of the project or 5 years (whichever is earlier) from the date on which the project was approved and for the projects continuing for longer than 5 years, renewal will be mandatory. For renewal, the PI would be required to submit renewal request before expiry of approved period otherwise the approval would be deemed to have stopped upon expiry.

Procedures for Appeal after Rejection of the proposal

For research proposals rejected by the Committee, the applicant may appeal for a repeat review in writing, within Twelve (12) weeks of the receipt of the Committee's decision. While doing so, the applicant shall give justification relevant to the issues / objections raised by the Committee.

18. Amendments to the Approved Research Proposal and Informed Consent Documents

- All amendments to the approved research proposal shall be submitted to the Committee immediately for its review.
- No changes in the protocol and/ or Informed Consent Documents shall be initiated without prior written approval from the Committee, except when necessary to eliminate immediate hazards to the subjects, or when the change(s) involve only logistical or administrative aspects of the proposal [e.g. change of telephone number(s)].

19. Research studies that are Exempt Ethical approval:

Within the definition of research, the following are not considered to be 'research' and would be exempt:

- Service evaluation
- Performance reviews
- Literary or artistic criticism
- Testing within normal education requirements
- Quality assurance/audit projects that do not involve access to or collection of private or sensitive data

20. Procedure for decision making regarding the research project involving vulnerable population

Vulnerable persons are those individuals who are relatively or absolutely incapable of protecting their own interests and providing valid informed consent. Include economically and socially disadvantaged; children (up to 18 years);women in special

situations; tribals and marginalized communities; refugees, migrants, homeless, persons or populations in conflict zones, riot areas or disaster situations; afflicted with mental illness and cognitively impaired individuals, differently abled – mentally and physically disabled; terminally ill or are in search of new interventions having exhausted all therapies; suffering from stigmatizing or rare diseases; or have diminished autonomy due to dependency or being under a hierarchical system and 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.

In making decision on application for the ethical review of research proposal involving vulnerable population, ISI-RCPRRH will consider the following:

- ISI-RCPRRH will carefully determine the benefits and risks of the study and examine the justification provided and risk minimization strategies
- Additional safety measures should be strictly reviewed and approved by the ISI-RCPRRH.
- ISI-RCPRRH must ensure that the informed consent process should be well documented and recording of assent in case of research studies involving children aged 7 to 18 years and reconsent, when applicable.
- Informed consent from vulnerable populations may be obtained from LAR (Legally authorized representative) in presence of impartial witness after through explanation of risks and benefits.
- A decision will only be taken when sufficient time has been allowed for the review and discussion of an application in the absence of non-members (e.g. PI and CoIs) from the meeting.
- Decision will only be taken at meetings where a quorum is complete.
- Decision will be taken only after reviewing a complete application with all the required documents
- Decision will specify the conditional decision if any, with clear suggestions and rereview procedure.
- Rejection of proposal will be supported by clearly stated reasons.

21. Procedure for communicating the decision of ISI-RCPRRH to the Investigator

- A decision of the ISI-RCPRRH will be communicated to the applicant in writing, within 14 days of the meeting at which the decision was taken. The minutes will be circulated to all the guides/supervisors in case of student proposals.
- All the approvals will be valid for only five years or for the duration of the project whichever is less. Investigator has to get his or her project re-approved after five years, if necessary.
- An investigator is expected to submit a reply to the letter of recommended modifications / queries sent by the ISI-RCPRRH, within 30 days of date of receipt of the letter. If the investigator fails to reply within this period, the file will be considered closed by the ISI-RCPRRH and ethics clearance certificate will not be issued by ISI-RCPRRH. The investigator will have to re-apply for the ethics committee approval.
- Applicant(s) need to collect a certificate of approval from the ISI-RCPRRH office/ ISI-RCPRRH Member Secretary/Convener.

The communication of the decision will include:

- Name and address of ISI-RCPRRH.
- The date and place of decision.
- The name and designation of the applicant.
- Title of the research proposal reviewed.
- The clear identification of proposal no., version no., date, amendment no., date.
- A clear statement of decision reached.
- Any advice by the ISI-RCPRRH to the applicant.
- In case of conditional decision, any requirement by ISI-RCPRRH, including suggestions for revision, and the procedure for having the application re reviewed.

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

22. Procedure for follow-up of research projects by Ethics Committee

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

Following instances and events will require the follow-up review:

- Any protocol amendment likely to affect rights, safety or well-being of research subject.
- Serious or unexpected adverse effect of action taken by Investigator, Sponsor and Regulatory Authority.
- Any event or verified information that may affect the benefit/risk ratio of the study.
- A decision of a follow up review will be issued and communicated to the applicant indicating modification/suspension/termination /continuation of the project.
- In case of premature suspension /termination of a project, the applicant must notify the ISI-RCPRRH of the reasons for suspension/termination with a summary of results.
- Applicant (non-thesis project) must inform the time of completion of study and must send the result summary to ISI-RCPRRH. ISI-RCPRRH must receive a copy of final summary of study completed from the applicant.

23. Procedure for documentation and archiving of documents and communications of ISI-RCPRRH

- All the documents and communications of ISI-RCPRRH will be dated, filed and archived in ISI-RCPRRH office.
- Only persons, who are authorized by the Chairman of ISI-RCPRRH, will have the access to the various documents.
- All the documents related to research proposals will be archived for a minimum period of 5 years in the Institute, following the completion /termination of the study.
- No document (except agenda) will be retained by any ISI-RCPRRH member.
- At the end of each meeting, every member must return all the research proposals and documents to ISI-RCPRRH office staff. They will archive one copy in ISI-RCPRRH office and other copies will be destroyed after one year.

Following documents will be filed and archived with proper label on the top of file

- The constitution, written standard operating procedures of the ISI-RCPRRH, and regular (annual) reports.
- The curriculum vitae of all ISI-RCPRRH members.
- A record of all expenses if any, of the ISI-RCPRRH, including allowances and reimbursements made to the secretariat and ISI-RCPRRH members.
- The published guidelines for submission established by the ISI-RCPRRH.

Following documents will be files and archived for easy identification of proposal.

- The agenda of the ISI-RCPRRH meetings.
- The minutes of the ISI-RCPRRH meetings.
- One copy of all material submitted by an applicant.
- A copy of the decision and any advice or requirements sent to an applicant.
- All written documentation received during the follow-up.
- The notification of completion, premature suspension, or premature termination of study.

24. Responsibility of researchers

- The researcher should only use the ISI-RCPRRH approved version of the consent form, including its local translations.
- Adequate information necessary for informed consent should be communicated in a language and manner easily understood by prospective participants.
- In case of differently abled participants, such as individuals with physical, neurological or mental disabilities, appropriate methods should be used to enhance the participants' understanding, for example, braille for the visually impaired.
- There should be no restriction on the participant's right to ask questions related to the study or to discuss with family and friends or take time before coming to a decision.
- The researcher should not give any unjustifiable assurances or influence or intimidate a prospective participant to enroll in the study.
- The researcher must ensure that the participant is competent and has understood all aspects of the study and that the consent is given voluntarily. Where the participant and/or the legally acceptable representative (LAR) are illiterate, an impartial literate person, not connected to the research, should be present throughout the consent process as witness.
- The researcher should administer a test of understanding whenever possible for sensitive studies. If need be, the test may be repeated until the participant has really understood the contents.
- When a participant is willing to participate but not willing to sign or give a thumb impression or cannot do so, then verbal/oral consent may be taken on approval by the ISI-RCPRRH, in the presence of an impartial witness who should sign and date the consent document. This process can be documented through audio or video recording of the participant, the PI and the impartial witness, all of whom should be seen in the frame. However, verbal/oral consent should only be taken in exceptional circumstances and for specific,

justifiable reasons with the approval of the ISI-RCPRRH. It should not to be practiced routinely.

- The researcher must assure prospective participants that their decision whether or not to participate in the research will not affect their rights, the patient–clinician relationship or any other benefits to which they are entitled.
- Reimbursement may be given for travel and incidental expenses/participation in research after approval by the ISI-RCPRRH.
- The researcher should ensure free treatment for research related injury (disability, chronic life-threatening disease and congenital anomaly or birth defect) and if required, payment of compensation over and above medical management by the investigator and/institution and sponsor(s), as the case may be.
- The researcher should ensure that the participant can continue to access routine care even in the event of withdrawal of the participant.
- Re-consent or fresh informed consent of each participant must be taken under the circumstances as described in Section 26 of this document.

25. Informed consent process

The researcher must obtain voluntary written informed consent from the prospective participant for any biomedical and health research involving human participants. This requirement is based on the principle that competent individuals are entitled to choose freely whether or not to participate or continue to participate in the research. Informed consent is a continuous process involving three main components

- providing relevant information to potential participants,
- ensuring competence of the individual,
- ensuring the information is easily comprehended by the participants and assuring voluntariness of participation.

Informed voluntary consent protects the individual's freedom of choice and respects the individual's autonomy.

Requisites

- The participant must have the capacity to understand the proposed research, be able to make an informed decision on whether or not to be enrolled and convey her/his decision to the researcher in order to give consent.
- The consent should be given voluntarily and not be obtained under duress or coercion of any sort or by offering any undue inducements.
- In the case of an individual who is not capable of giving voluntary informed consent, the consent of LAR must be obtained.
- It is mandatory for a researcher to administer consent before initiating any study related procedures involving the participant.
- It is necessary to maintain privacy and confidentiality of participants at all stages.

An informed consent form must include the following:

- Statement mentioning that it is research
- Purpose and methods of the research in simple language
- Expected duration of the participation and frequency of contact with estimated number of participants to be enrolled, types of data collection and methods
- Benefits to the participant, community or others that might reasonably be expected as an outcome of research
- Any foreseeable risks, discomfort or inconvenience to the participant resulting from participation in the study
- Extent to which confidentiality of records could be maintained, such as the limits to which the researcher would be able to safeguard confidentiality and the anticipated consequences of breach of confidentiality
- Payment/reimbursement for participation and incidental expenses depending on the type of study
- Free treatment and/or compensation of participants for research-related injury and/or harm

- Freedom of the individual to participate and/or withdraw from research at any time without penalty or loss of benefits to which the participant would otherwise be entitled
- The identity of the research team and contact persons with addresses and phone numbers (for example, PI/Co PI for queries related to the research and Chairperson/Member Secretary/Convener or helpline for appeal against violations of ethical principles and human rights).

In addition, the following elements may also be required, depending on the type of study:

- Any alternative procedures or courses of treatment that might be as advantageous to the participant as the ones to which she/he is going to be subjected
- If there is a possibility that the research could lead to any stigmatizing condition, for example HIV and genetic disorders, provision for pre-test and post-test counselling
- Insurance coverage if any, for research-related or other adverse events
- Foreseeable extent of information on possible current and future uses of the biological material and of the data to be generated from the research. Other specifics are as follows:
  - period of storage of the sample/data and probability of the material being used for secondary purposes.
  - whether material is to be shared with others, this should be clearly mentioned.
  - right to prevent use of her/his biological sample, such as DNA, cell-line, etc., and related data at any time during or after the conduct of the research.
  - risk of discovery of biologically sensitive information and provisions to safeguard confidentiality.
  - post research plan/benefit sharing, if research on biological material and/or data leads to commercialization.

- Publication plan, if any, including photographs and pedigree charts.

26. Documentation of informed consent process

- Each prospective participant should sign the informed consent form after going through the informed consent process of receiving information, understanding it and voluntarily agreeing to participate in the research.
- In case the participant is incompetent (medically or legally) to give consent, the LAR's consent must be documented.
- The process of consent for an illiterate participant/LAR should be witnessed by an impartial literate witness who is not a relative of the participant and is in no way connected to the conduct of research, such as other patients in the ward who are not in the study, staff from the social service department and counsellors. The witness should be a literate person who can read the participant information sheet and consent form and understand the language of the participant.
- If the participant cannot sign then a thumb impression must be obtained.
- The researcher who administers the consent must also sign and date the consent form.
- In the case of institutionalized individuals, in addition to individual/LAR consent, permission for conducting the research should be obtained from the head of that institution.
- In some types of research, the partner/spouse may be required to give additional consent.
- In genetic research, other members of a family may become involved as secondary participants if their details are recorded as a part of the family history. If information about the secondary participants is identifiable then their informed consent will also be required.
- Online consent may be obtained, for example, in research involving sensitive data such as unsafe sex, high risk behaviour, use of contraceptives (condoms, oral pills), or emergency contraceptive pills among unmarried females in India etc. Investigators must ensure that privacy of the participant and confidentiality of related data is maintained.

27. Re-consent or fresh consent

Re-consent or fresh informed consent of each participant must be taken under the following circumstances:

- new information pertaining to the study becomes available which has implications for participant or which changes the benefit and risk ratio;
- a research participant who is unconscious regains consciousness or who had suffered loss of insight regains mental competence and is able to understand the implications of the research;
- a child becomes an adult during the course of the study;
- research requires a long-term follow-up or requires extension;
- there is a change in treatment modality, procedures, site visits, data collection methods or tenure of participation which may impact the participant's decision to continue in the research; and
- there is possibility of disclosure of identity through data presentation or photographs (this should be camouflaged adequately) in an upcoming publication.
- the partner/spouse may also be required to give additional re-consent in some of the above cases.

28. Waiver of consent

The researcher can apply to the ISI-RCPRRH for a waiver of consent if the research involves less than minimal risk to participants and the waiver will not adversely affect the rights and welfare of the participants.

The ISI-RCPRRH may grant consent waiver in the following situations:

- research cannot practically be carried out without the waiver and the waiver is scientifically justified;
- retrospective studies, where the participants are de-identified or cannot be contacted;
- research on anonymized biological samples/data;
- certain types of public health studies/surveillance programmes/programme evaluation studies;

- research on data available in the public domain; or
- research during humanitarian emergencies and disasters, when the participant may not be in a position to give consent. In such cases, attempt should be made to obtain the participant's consent at the earliest.

29. Management of Premature Termination / Suspension / Discontinuation of the Study / Withdrawal of the Study

Protocols may be terminated at the recommendation of the ISI-RCPRRH, Principal Investigator, sponsor, Regulator or other authorized bodies wherein subject enrolment and subject follow-up are discontinued before the scheduled end of the study.

It is the responsibility of the Chairman to terminate any study that the ISI-RCPRRH has previously approved when the safety or benefit of the study participants is doubtful or at risk, also to review the termination suggested by ISI-RCPRRH members, PI, Sponsor or other authorized bodies. The secretariat is responsible for management of the premature termination/ suspension/discontinuation documents/Withdrawal of study.

On receiving notice of premature termination/ Suspension / Discontinuation of the study / Withdrawal of study before site initiation of a research study:

- The member secretary/Convener / Chairman shall review the results, reasons and accrual data and discuss the report at the regular Full Board meeting.
- If the Premature termination / suspension /discontinuation Report is unclear or more information is required from the PI, the Chairman shall instruct the Secretariat to seek clarifications/ additional information from the Principal Investigator.
- The Chairman /Member Secretary/Convener/ ISI-RCPRRH members will review the information available and take a decision depending on the seriousness of the termination. The decision will be taken to ensure that the

safety and rights of the research participants are safeguarded. The decision will be taken by consensus / voting (> 66% of the members).

30. Review & request for Revision of the Existing SOP

- Any member of ISI-RCPRRH or Investigator of ISI who notices any inconsistency or has any suggestion on how to improve a procedure should communicate through the Member Secretary/Convener/Chairman of the ISI-RCPRRH.
- If ISI-RCPRRH agree with the request then appropriate team will be designated by the Director, ISI and Chairman, ISI-RCPRRH to proceed with the revision process.
- If Committee does not agree, the Member Secretary/Convener will inform the person who made the request for the decision.
- The Member Secretary/Convener will regularly prepare the amendment or addendum (if any) to the existing SOP to the approved discussion points in the ISI-RCPRRH meetings.
- The Member Secretary/Convener will review the SOP at least once in every two years and incorporate the addendum and record the date of review in the SOP master file.

Annexure: 01

CONFIDENTIALITY AGREEMENT

I hereby do confirm that to maintain the integrity and sanctity in the best interests of the committee, I must volunteer to inform the chairperson/ Secretary and other members to withdraw myself from participating in any process that might lead to possible personal benefit owing to my presence as an opining and decision making member of the ISI-RCPRRH during any of the meetings of the ISI-RCPRRH in order to avoid the conflict of interest involved. I also do hereby declare that I will not breach the confidentiality and all the information that is accessible to me as a member of ISI-RCPRRH, especially during the reviewing, decision making and any discussion, shall not be disclosed by me to anyone other than the members of the committee or concerned study related personnel, as approved by the regulatory body.

Signature:

Name & Designation: _____

_____

Date: _____/_____/_____

Annexure: 02

UNDERTAKING REGARDING CONFLICT OF INTEREST

Date:

To

The Chairperson,

Review Committee for Protection of Research Rights to Humans,

ISI, Kolkata.

I _____, hereby declare that as Principal Investigator/ Co-investigator / Author / Study team member (of) / I have financial interest in the study entitled _____

_____

_____

_____

_____ and

I realize that there is a possibility of evoking a conflict of interest I will voluntarily withdraw from this meeting after informing the Chairperson in advance and in writing about it.

Sincerely,

Signature

Name: _____

Role in ISI-RCPRRH: _____

Date of meeting: _____/ _____/ _____

Annexure: 03

CONFIDENTIALITY AGREEMENT

I do hereby declare to maintain confidentiality and agree to the following: -

1. I understand that my name will be recorded on official records in connection with access to any IEC information / data retained by ISI-RCPRRH Secretariat.
2. I will maintain the privacy and confidentiality of all accessible data (electronic & printed) or spoken confidential information.
3. I will access data only for which I am authorised explicitly. On no occasion will I use this data including personal, confidential, or subject information for my personal interest or advantage or for any other purpose.
4. I will not disclose confidential or personal data or sensitive information to anyone other than those to whom I am authorised to do so.
5. All personal or confidential information will be kept secure while in my custody and no copies or notes containing such information will be retained by me on completion of the agreed duties.
6. I agree to protect the confidentiality and security of any password, resources used by me to access and utilize the computer systems.
7. I will lock away any record when I leave the office or workstation.
8. If in doubt about any aspect of handling confidential or personal information, I will inform the Member Secretary/Convener or any authorized person.
9. I understand that I will continue to be bound by this signed Confidentiality Agreement.

Signature of Coordinator/Office assistant: _____

Date: _____/_____/_____

Name: _____

Signature of Member Secretary/Convener: _____

Date: _____/_____/_____

Name: _____

Annexure: 04

REQUEST FOR REVIEW AND APPROVAL OF RESEARCH PROJECT INVOLVING HUMANS

To: THE REVIEW COMMITTEE FOR PROTECTION OF RESEARCH RISKS TO HUMANS, Indian Statistical Institute, Kolkata 700 108

[*This form must be filled, signed and submitted by the Principal Investigator of the project for which ethical approval is being sought.*]

1. Name, Designation and Address of the Principal Investigator*:

* *The Principal Investigator must be the person who assumes responsibility on all aspects – scientific and ethical – of the proposed project.*

2. Names, Designations and Addresses of all Collaborating Investigators:

3. Project Title and Name of Funding Agency:

4. Research Objectives, Study Design, Materials and Methods of Data and Sample Collection (Attach separate sheets, if necessary):

5. Is the Project ongoing?:

6. (Expected/Actual) Starting Date of the Project:

7. Expected Duration of the Project:

8. Particulars of human participants of this research project:

8.1 Are individuals of any specific age-group to be excluded?
If yes, provide justification:

8.2 Are individuals of any gender (male/female) to be excluded?

8.3 Are individuals with any handicap (physical or mental) to be excluded?
If yes, provide justification:

8.4 Are individuals belonging to any particular community/social-group to be excluded?
If yes, provide justification:

8.5 Are individuals resident in any specific geographical region to be excluded?

If yes, provide justification:

9. Describe the nature of information to be collected from each participant (If possible, attach a copy of the Questionnaire/Schedule to be used in the project.)

10. Who will collect the information?

11. Will any biological material (blood, tissue, etc.) be collected?

If yes, specify the nature of material:

12. Who will collect the biological material?

13. List the potential risks of collection of biological materials from the study participants:

14. Will appropriate precautions be taken to minimize physical risks, including of infection, to each participant of collection of biological material?

    If yes, describe the steps to be taken:

15. Will participants be administered any substance/drug or exposed to any radiation/magnetic field, etc. during the Project?

    If yes, provide the name of the substance/drug, describe its nature and indicate whether adequate safety certificates have been taken from any competent authority (e.g., Drug Controller of India):

16. Will each participant be informed of the risks and benefits of participation in the Project prior to collection of information/biological-material?

17. Will the information/biological-material be collected with voluntary informed consent of each participant?

    If yes, specify the method of documentation of informed consent (If possible, enclose a copy of the Consent Form):

18. Will each participant, even after providing consent at the time of collection of information/biological-material, have the right, at any time during or after the conclusion of the Project, to:

    (i) withdraw?

    (ii) request for destruction of information/biological-material collected from her/him?

If No to either of 17(i) or 17(ii), provide reasons:

19. Will participants be paid for their participation in the Project?

    If Yes, form and amount of payment to be made to each participant:

20. Will primary information/biological-materials be available to others in a form by which they may be able to obtain identifying information of the participant?

    If yes, specify reasons:

21. Will any participant be contacted more than once during the Project?

    If yes, who will make the second and subsequent contacts?

22. Will data be stored beyond the date of completion of the project?

    If yes, (a) how will the data be stored?

    (b) will identifying information be available from the stored data?

23. Will biological samples be stored beyond the date of completion of the project?

    If yes, (a) how will the samples be stored?

    (b) will identifying information be available from the stored samples?

    (c) will the samples be irretrievably coded?

    (d) if samples are not irretrievably coded, what procedures will be adopted to ensure that the code cannot be broken by others?

24. Is there any foreseeable possibility of filing any patent/copyright from the information or biological-material (even if value-added by you or your collaborators through experimentation or otherwise) collected in this Project?

25. Will any commercial use be made by you or your collaborators of the information or biological materials collected in this Project?

26. If the answer to (24) or (25) is "Yes", will financial benefits be shared with each participant?

    If yes, describe the method of benefit-sharing by you or your collaborators:

27. Will results of the project be shared?
    27.1 With each participant:

    27.2 With the community/group:

28. If results at the individual-level are to be shared with the corresponding participant, will her/his consent be taken before sharing the results?

29. Will information or samples be sent outside of India?

30. If Yes to (29), will Govt. of India regulations pertaining to despatch of information or samples to outside of India be followed?

Date: Signature of the Principal Investigator

Date: Signature of the Supervisor (if the applicant is student)