19.1. Purpose

This Standard Operating Procedure (SOP) describes the requirements and process of review of research that involves vulnerable participants.

19.2. Scope

This SOP covers the policies and procedures applied to all research proposals submitted to the IEC that involve vulnerable participants.

19.3. Responsibility

- It is the responsibility of the Member Secretary with Secretariat to maintain up-to-date tools, like checklists, for reviewing research concerning vulnerable groups based on new and evolving applicable regulations and guidelines.
- IEC Chairperson/Member Secretary are responsible for ensuring that IEC members are well-versed in new and evolving regulations and guidelines pertaining to vulnerable populations, through regular training programmes.
- The Member Secretary/Chairperson is responsible for selecting primary reviewers with appropriate expertise to conduct the reviews of such research and for identifying consultants having expertise for specific review as and when required.
- IEC members are responsible for review of research planned for vulnerable populations, including an assessment of potential for coercion.

19.4. Definition and Mandate

19.4.1 Definition

Vulnerable Subjects: Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, and patients in emergency situations,

ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent.

19.4.2 Mandate

Gazette notification dated 19th March, 2019 [G.S.R. 227(E)] has mandated audio-visual recording of informed consent process in case of vulnerable participants in clinical trials of new chemical entity/ new molecular entity. The IEC should exercise particular care to protect the rights, safety and well-being of all vulnerable subjects participating in the study,

19.5. Detailed instructions

19.5.1. Reviewing protocols with vulnerable participants

- The protocol should be reviewed following the procedure prescribed from time to time. Additionally, the protocol should be reviewed to assess whether the following points are addressed:
    - Can the research be performed in any other non-vulnerable participants?
    - Is there justification to use vulnerable population?
    - Do the benefits justify the risks?
    - Are the participants selected equitably?
- Have the measures to protect Autonomy of the vulnerable population been described?
- IEC members dealing with such protocols should be well versed with the potential harm or risk of such population participating in the study.
- The review must address all points in the checklists for different vulnerable populations.

19.5.3. Appointing Reviewers

The Member Secretary/Chairperson will appoint two or more members of the IEC who have a thorough understanding of the ethical review process and experience in the field of research to review such type of protocols.

19.5.4. Duties of Secretariat

- Provide a suitable checklist to the investigator depending on the type of participants to be recruited for the study.

- Provide appropriate reference material including National Ethical Guidelines of ICMR, 2017 or help reviewer locate the material relevant to vulnerable populations when specifically requested for, by a reviewing member.

19.5.5. Responsibilities of Reviewers

- IEC Members will review the protocol and the informed consent document or assent form as per SOPs.
- The IEC members will discuss the comments in the IEC meeting and letter regarding approval/modification/ disapproval will be sent to the PI.
- The discussion will be documented in the minutes.
- The Member Secretary will ensure that the IEC recommendations have been incorporated in the revised protocol and protocol related documents.

10.5.6. Approval of the protocol

- The final version of the protocol will be approved at a full committee meeting.
- Wherever necessary the IEC approval should state that if in future the vulnerability status of the participant's changes, for e.g. unconscious patient gaining consciousness or a schizophrenic patient regains insight, the participant will be re-consented.

19.6. Annexure

NOTE: The following annexure apply to some sections of vulnerable participants. These checklists should be filled in by principal investigator and should be reviewed by IEC members. Appropriate modifications should be made as per individual IEC requirement

Annexure 1: AX 01/SOP19/V1 – Checklist: Requirements for Research Involving Children

Annexure 2: AX 02/SOP 19/V1 - Checklist: Requirements for Research Involving Pregnant Women & Foetuses

Annexure 3: AX 03/SOP 19/V1 - Checklist: Research Involving Cognitively Impaired Adults

Annexure 4: AX 04/SOP 19/V1- Checklist-Research Involving Students, Employees or Residents

Annexure 5: *AX 05/SOP 19/V1*- Checklist: Considerations for Genetic Research

Annexure 1: AX 01/SOP 19/V1

Checklist: Requirements for Research Involving Children

Name of Principal Investigator:

Study Title:

For the principal investigator		IEC Office
RISK DETERMINATION	BENEFIT ASSESSMENT	IEC ACTION
☐Minimal *	Direct benefit Indirect benefit to community/ society	Approvable
☐Minor increase over minimal risk (low risk) Greater than minimal risk (high risk)	☐ Potential benefit to child	Approvable
☐Greater than minimal risk	Indirect benefit, offer knowledge about child's condition/disorder	Approvable on case –by- case basis**

* Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life of a healthy individual or occurring during the performance of routine physical or psychological examinations or tests.

** Consent of both parents may be needed as applicable.

	Yes	No	NA
Does the research pose greater than minimal risk to children?			
If yes: Are convincing scientific and ethical justifications given?			
If yes: Are adequate safeguards in place to minimize these risks?			
Does the study involve healthy children?			
If yes: Is the inclusion of healthy children justified?			
Are the studies conducted on animals and adults appropriate and justified?			
If No: Is the lack of studies conducted on animals and adults justified?			
Will older children be enrolled before younger ones?			
Is permission of both parents necessary?			
If Yes: Are conditions under which one of the parents may be considered: “not reasonably available” described?			
If Yes: Are the conditions acceptable?			
Will efforts be made to ensure that parents’ permission to involve their children in research studies is free from coercion, exploitation, and/or unrealistic promises?			
Are provisions made to obtain the oral assent of children over 7 and up to 12, honouring their dissent?			
Are provisions made to obtain the written assent of children over 12 and up to 18, honouring their dissent?			

Are provisions made to protect participants' privacy and the confidentiality of information regarding procedures?			
Are there special problems that call for the presence of a monitor or IEC member during consent procedures?			
Are special needs of adolescents such as counselling and confidentiality accounted for in the research design?			
Are there any special problems such as confidentiality and reporting that might arise in sensitive research about child abuse or sexual practices of teenagers?			
Does the research involve possibility of findings which may have implications for other family members? (for eg. genetic risk, HIV infection, Hepatitis C)			
If Yes: Are there adequate mechanisms in place to deal with other members of the family?			
Are parents required to be present during the conduct of the research? (Are proposed participants' very young?)			

Signature of Principal Investigator: _____ Date _____

IEC Office use only
Comments of Primary Reviewer:
Primary Reviewer Signature and Date

Annexure 2: AX 02/SOP 19/V1

Checklist: Requirements for Research Involving Pregnant Women and Foetuses

Name of Principal Investigator:

Study Title:

When research involves pregnant women or foetuses

	Yes	No	NA
Where scientifically appropriate preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and foetuses?	☐	☐	☐
Is the risk to the foetus not greater than minimal, or any risk to the foetus which is greater than minimal caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the foetus?	☐	☐	☐
Any risk that is the least possible for achieving the objectives of the research.	☐	☐	☐
Is the woman's consent or the consent of her legally authorized/acceptable representative obtained in accordance with the informed consent provisions, unless altered or waived?	☐	☐	☐
Is the woman or her legally authorized/acceptable representative, fully informed regarding the reasonably foreseeable impact of the research on the foetus or resultant child?	☐	☐	☐
Will any inducements, monetary or otherwise, be offered to terminate a pregnancy?	☐	☐	☐
Do individuals engaged in the research have a part in any decisions as to the timing, method, or procedures used to terminate a pregnancy?	☐	☐	☐
Do individuals engaged in the research have a part in determining the viability of a foetus?	☐	☐	☐

When research involves neonate after delivery

	Yes	No	NA

1. Are scientifically appropriate, preclinical, and clinical studies, conducted and provide data for assessing potential risks to neonates?	□	□	□
2. Is the individual providing consent, fully informed regarding the reasonably foreseeable impact of the research on neonate?	□	□	□
3. Will any inducements, monetary or otherwise, be offered to terminate a pregnancy?	□	□	□
4. Do individuals engaged in the research have a part in any deciding as to the timing, method, or procedures used to terminate pregnancy?	□	□	□
5. Do individuals engaged in the research have a part in determining the viability of a foetus?	□	□	□

A. Foetuses of uncertain viability	**Yes**	**No**	**NA**
1. Does the research hold out the prospect of enhancing the probability of survival of the particular foetus to the point of viability, and is any risk least possible for achieving the objectives of the research?	□	□	□
OR The purpose of the research is development of important biomedical or healthcare knowledge which cannot be obtained by other means. Will there be a risk to the foetus from the research?	□	□	□
2.Is the legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence or temporary incapacity, the legally effective informed consent of either parent's legally authorized/acceptable representative obtained?	□	□	□
B. Nonviable foetuses	Yes	No	NA
1. Will vital functions of the neonate be artificially maintained?	□	□	□
2. Is there any risk to the neonate resulting from the research?	□	□	□
3.The purpose of the research is the development of important biomedical and healthcare knowledge that cannot be obtained by other means; and	□	□	□

4. The legally effective informed consent of both parents of the neonate will be obtained (waiver and alteration provisions do not apply here). However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable foetus will suffice to meet the requirements of this paragraph. (The consent of a legally authorized/ acceptable representative of either or both of the parents of a nonviable foetus will not suffice to meet the requirements of this paragraph.)	☐	☐	☐

<u>This type of research can be conducted only after The IEC finds that</u>

(a) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women and/or foetuses**.**

(b) The research will be conducted in accordance with applicable regulatory and ethical guidelines.

Signature of Principal Investigator: _____ Date _____

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Comments of Primary Reviewer:	
Primary Reviewer's Signature and Date	

Annexure 3: AX 03/SOP 19/V1

Checklist- Research Involving Cognitively Impaired Adults

Name of Principal Investigator:

Study Title:

1.Research Involving Cognitively Impaired Adults in which there is Anticipated Direct Benefit to the participant (All items must be "Yes")	
□ Yes □ No	Is the recruitment of participants justified considering the rationale and objectives of the study?
□ Yes □ No	The risk is justified by the anticipated benefit to the participants.
□ Yes □ No	The relation of anticipated benefit to the risk is at least as favourable to the participants as that presented by available alternative approaches.
□ Yes □ No	Will the participants be withdrawn if they appear to be unduly distressed?
□ Yes □ No	The proposed plan for the assessment of the capacity to consent is adequate.
□ Yes □ No	Consent will be taken from participants capable of being consulted.
□ Yes □ No	Does the consent document include provision for a legally authorized/acceptable representative in case participants are not capable of being consulted?

2. Research Involving Cognitively Impaired Adults in which there is No Anticipated Direct Benefit to the participant (All items must be "Yes")		
☐ Yes	☐ No	Is the recruitment of participants justified considering the rationale and objectives of the study?
☐ Yes	☐ No	Are the foreseeable risks to the participants low?
☐ Yes	☐ No	Is the negative impact on the participant's well-being minimized and low?
☐ Yes	☐ No	Will the participants be particularly closely monitored?
☐ Yes	☐ No	Will the participants be withdrawn if they appear to be unduly distressed?
☐ Yes	☐ No	The proposed plan for the assessment of the capacity to consent is adequate.
☐ Yes	☐ No	Consent will be taken from participants capable of being consulted.
☐ Yes	☐ No	Does the consent document include provision for a legally authorized/acceptable representative in case participants are not capable of being consulted?

Signature of Principal Investigator: _____ Date _____

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Comments of Primary Reviewer	
Primary Reviewer Signature and Date	

Annexure 4: AX 04/SOP 19/V1

Checklist: Research Involving Students, Employees, or Residents

Name of Principal Investigator:

Study Title:

Have the participants been assured that their status (education, employment, and/or promotion) will not be affected by any decision to participate or not?	☐ No	☐ Yes
Have the risks to participants been minimized?	☐ No	☐ Yes
Have participants been assured that participation is voluntary (no signs of coercion)?	☐ No	☐ Yes
Have participants been assured that privacy and confidentiality will be protected?	☐ No	☐ Yes

Answers to all the above points should be YES for approval

Signature of Principal Investigator: _____ Date _____

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Comments of Primary Reviewer	
Primary Reviewer Signature and Date	

Annexure 5: AX 05/SOP 19/V1

Checklist: Considerations for Genetic Research

Name of Principal Investigator:

Study Title:

	Yes	No
1. Will the samples be made anonymous to maintain confidentiality? If yes, then the following checklist points are not applicable	☐	☐
2. Will the results be disclosed? a) If yes, has the investigator established clear guidelines for disclosure of information, including interim or inconclusive research result? b) Will the results be used in management of current condition of patient?	☐	☐
3. Has the appropriateness of the various strategies for recruiting participants and their family members been considered?	☐	☐
4. Does the proposed study population comprise family members?	☐	☐
5. Will family members be implicated in the studies without consent?	☐	☐
6. Will the samples be destroyed in the future?	☐	☐
7.Will the samples be used for future research	☐	☐
8. Is pre-test and post-test genetic counselling being offered?	☐	☐

Signature of Principal Investigator: _____ Date _____

IEC Office use only	
Comments of Primary Reviewer	
Primary Reviewer Signature & Date	

19.7. Flow Chart

No.	Activity	Responsibility
1	Appoint reviewers	Chairperson/ Member Secretary
2	Review the protocol	IEC members
3	Discussion at IEC meeting	IEC member
4	Communicating the decisions to principal investigator	IEC Secretariat