Title: Reviewing Proposals Involving Vulnerable Populations

SOP Code: SOP 19/V2
Effective Date: 21-10-2019

SOP Constitution and Approval:

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1. Purpose

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

2. Scope

This SOP covers the policies and procedures applied to all research dealing with vulnerable participants submitted to the IHEC.

3. Responsibility

- It is the responsibility of the Member Secretary/Additional 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.
- IHEC Chairperson / Member Secretary/Additional Member Secretary are responsible for ensuring that IHEC members are well-versed in new and evolving regulations and guidelines pertaining to vulnerable populations, through regular training programmers.
- The Additional Member Secretary/ Member Secretary/ Chairperson is responsible for selecting primary reviewers with appropriate expertise to conduct the reviews of such research and for securing consulting expertise as and when required for selected reviews.
- IHEC member is responsible for conducting review of research planned for vulnerable populations, including an assessment of potential for coercion.

4. Definition and Mandate

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, dental and nursing students, subordinate hospital and laboratory personnel. Other vulnerable subjects include patients with incurable diseases, unemployed or impoverished persons, patients in emergency situations, minority groups, homeless persons, nomads, tribal,

refugees, minors, pregnant women and fetus, children, socially, economically or politically disadvantaged and those incapable of giving consent(e.g. unconscious, differently abled persons).

4.2 Mandate

- Gazette notification by CDSCO dated 19th March 2019 has mandated audio-visual recording of informed consent process in case of vulnerable participants in clinical trials of new chemical entity/ new molecular entity

5. Detailed instructions

5.1. Reviewing protocols with vulnerable participants

- In addition to regular review process, the research protocol should be reviewed to assess if 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?
- IHEC 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 (Annexures 1 to 5- SOP 19/01).

5.2. Appointing Reviewers

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

5.3. 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 or help reviewer locate the material relevant to vulnerable populations when specifically requested for, by a reviewing member.

5.4. Responsibilities of Reviewers

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

5.5 Approval of the protocol

- The final version of the protocol will be approved at a full board meeting.
- Wherever necessary, the IHEC approval should state that if in future the vulnerability status of the participants' changes, for e.g. unconscious patient gaining consciousness or a schizophrenic patient regains insight, re-consent will be obtained from the participant.
- IHEC at the time of initial review or continuing review can suggest that routine monitoring may be conducted at more frequent intervals.

6. Annexures

NOTE: The following annexures apply to some sections of vulnerable participants. These checklists should be filled in by principal investigator and should be reviewed by IHEC members.

Annexure 1: AX01/SOP019/V2- Checklist: Requirements for research involving children

Annexure 2: AX02/SOP019/V2- Checklist: Requirements for research involving pregnant women & fetuses

Annexure 3: AX03/SOP019/V2- Checklist: Research involving cognitively impaired adults

Annexure 4: AX04/SOP019/V2- Checklist-Research involving students, employees or residents

Annexure 5: AX05/SOP019/V2- Checklist: Considerations for genetic research

Annexure 1: AX01/SOP019/V2

Checklist: Requirements for research involving children

Name of Principal Investigator:

Study Title:

S.no	Questions	Yes	No	NA
1.	Does the research pose greater than minimal risk to children?			
2.	If yes: Are convincing scientific and ethical justifications given?			
3.	If yes: Are adequate safeguards in place to minimize these risks?			
4.	Does the study involve healthy children?			
5.	If yes: Is the inclusion of healthy children justified?			
6.	Are the studies conducted on animals and adults appropriate and justified?			
7.	If No: Is the lack of studies conducted on animals and adults justified?			
8.	Will older children be enrolled before younger ones?			
9.	Is permission of both parents necessary?			
10.	If Yes: Are conditions under which one of the parents may be considered: "not reasonably available" described?			
11.	If Yes: Are the conditions acceptable?			
12.	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?			
13.	Are provisions made to obtain the assent of children over 7 and, where appropriate, honoring their dissent?			
14.	Are provisions made to protect participants' privacy and the confidentiality of information regarding procedures?			
15.	Are there special problems that call for the presence of a monitor or IHEC member during consent procedures?			
16.	Are special needs of adolescents such as counseling and confidentiality accounted for in the research design?			
17.	Are there any special problems such as confidentiality and reporting that might arise in sensitive research about child abuse or sexual practices of teenagers?			
18.	Does the research involve possibility of findings which may have implications for other family members?(for e.g. genetic risk, HIV infection, Hepatitis C)			
19.	If Yes: Are there adequate mechanisms in place to deal with other members of the family?			
20.	Are parents required to be present during the conduct of the research? (Are proposed participants' very young?)			

Signature of Principal Investigator: _____ Date _____

Comments of Primary Reviewer:

Primary Reviewer's Signature and Date:

Annexure 2: AX02/SOP019/V2

Checklist: Requirements for research involving pregnant women & fetuses

Name of Principal Investigator:

Study Title:

SECTION 1:THIS RESEARCH INVOLVES PREGNANT WOMEN OR FETUSES PRIOR TO DELIVERY

S no	Questions	Yes	No	NA
1.	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 fetuses?			
2.	Is the risk to the fetus not greater than minimal, or any risk to the fetuswhich is greater than minimal caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus?			
3.	Any risk that is the least possible for achieving the objectives of the research?			
4.	Is the woman's consent or the consent of her legally authorized representative obtained in accordance with the informed consent provisions, unless altered or waived?			
5.	Is the woman or her legally authorized representative, as appropriate, fully informed regarding the reasonably foreseeable impact of the research on the fetus or resultant child?			
6.	Will any inducements, monetary or otherwise, be offered to terminate a pregnancy?			
7.	Do individuals engaged in the research have a part in any decisions as to the timing, method, or procedures used to terminate a pregnancy?			
8.	Do individuals engaged in the research have a part in determining the viability of a fetus?			

If the response to any of the above is **NO**, the research should not be approved by the IHEC.

Signature of Principal Investigator: _____ Date _____

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Comments of Primary Reviewer:

Primary Reviewer's Signature and Date:

Name of Principal Investigator:

Study Title:

SECTION 2: THIS RESEARCH INVOLVES FETUSES AFTER DELIVERY

S.No.	Queries	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 decisions 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 fetus?			
6.	**In research involving fetuses of uncertain viability?**			
6a	Does the research hold out the prospect of enhancing the probability of survival of the particular fetus to the point of viability, and is any risk least possible for achieving the objectives of the research?			
6b	Or The purpose of the research is development of important biomedical knowledge which cannot be obtained by other means.			
7.	Will there be a risk to the fetus from the research?			
8.	Is the legally effective informed consent of either parent of neonate or, if neither parent is able to consent because of unavailability, incompetence or temporary incapacity, legally effective informed consent of either parent's legally authorized representative obtained?			
9.	**In research involving nonviable fetuses**			
9a	Will vital functions of the neonate be artificially maintained?			
9b	Is there any risk to the neonate resulting from the research?			
9c	The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means			
9d	The legally effective informed consent of both parents of the neonate will be obtained except that the waiver and alteration provisions do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable fetus will suffice to meet the requirements of this paragraph. (The consent of a legally authorized representative of either or both of the parents of a nonviable fetus will not suffice to meet the requirements of this paragraph.)			

If the response to any of above is **NO,** the research should not be approved by the IHEC.

<u>This type of research can be conducted only after The IHEC 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 fetuses

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: AX03/SOP019/V2
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")

	Items	Yes	No
A.	Is the recruitment of participants justified considering rationale and objectives of study?		
B.	Is the risk justified by anticipated benefit to the participants?		
C.	The relation of anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches.		
D.	Will the participants be withdrawn if they appear to be unduly distressed?		
E.	The proposed plan for the assessment of the capacity to consent is adequate.		

2. Research Involving Cognitively Impaired Adults in which there is No Anticipated Direct Benefit to the participant (All items must be "Yes")

	Items	Yes	No
A.	Is the recruitment of participants justified considering rationale and objectives of study?		
B.	Are the foreseeable risks to the participants low?		
C.	Is the negative impact on the participant 's well-being minimized and low?		
D.	Will the participants be particularly closely monitored?		
E.	Will the participants be withdrawn if they appear to be unduly distressed?		
F.	The proposed plan for the assessment of the capacity to consent is adequate.		
G.	Consent will be taken from participants capable of being consulted.		
H.	Does consent document include provision for legally acceptable representative in case the participants are not capable of being consulted?		

Signature of Principal Investigator: **Date:**

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Comments of Primary Reviewer:

Primary Reviewer's Signature and Date:

Annexure 4: AX04/SOP019/V2

Checklist-Research involving students, employees or residents

Name of Principal Investigator:

Study Title:

Research involving participants who are students, employees or residents require special considerations (All items must be "Yes")

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

Signature of Principal Investigator: **Date:**

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Comments of Primary Reviewer:

Primary Reviewer's Signature and Date:

Annexure 5: AX05/SOP019/V2

Checklist: Considerations for genetic research

Name of Principal Investigator:

Study Title:

Considerations for genetic research (All items must be "Yes")

Items	Yes	No
A. Will samples be made anonymous to maintain confidentiality? If yes, then the following checklist points are not applicable.		
B. Will the results be disclosed? If yes, a) 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?		
C. Has the appropriateness of the various strategies for recruiting participants and their family members been considered?		
D. Does the proposed study population comprise family members?		
E. Will family members be implicated in the studies without consent?		
F. Will the samples be destroyed in the future?		
G. Will the samples be used for future research?		
H. Is genetic counseling being offered?		

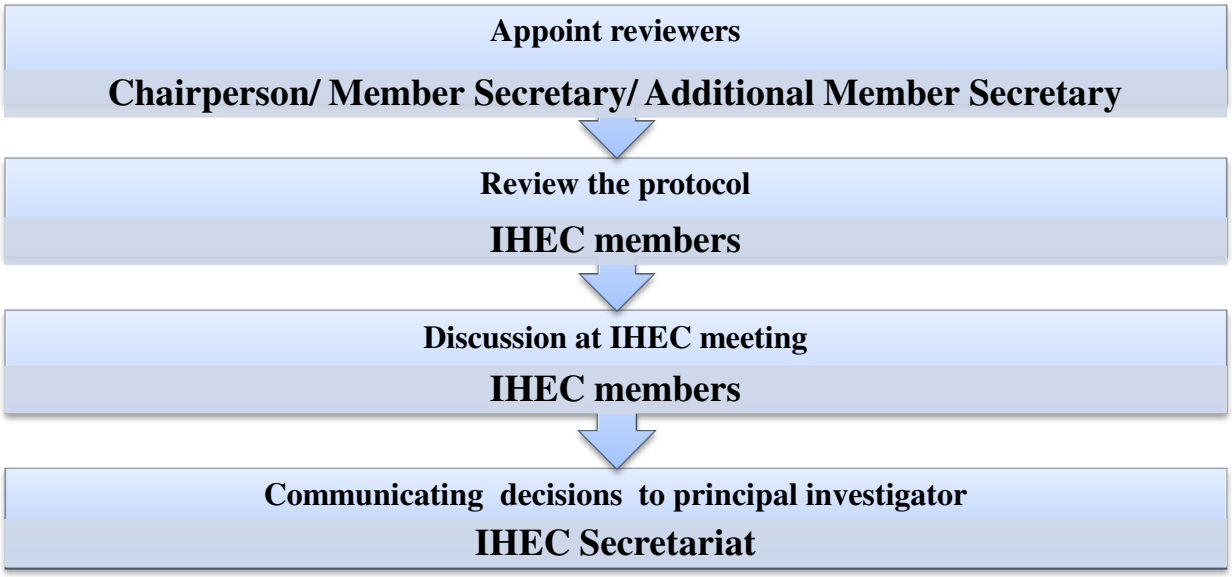
Signature of Principal Investigator: **Date:**

IHEC Office use only

Comments of Primary Reviewer:

Primary Reviewer's Signature and Date:

7. Flow Chart



8. References

- *Forum for Ethics review Committees in India (FERCI). Standard Operating Procedures of Institutional Ethics Committee (cited 5th October 2019). Available from: http://www.ferci.org/sops/*
- *Indian Council of Medical Research (ICMR). National Ethical guidelines for biomedical and health research involving human participants, October 2017 (cited 6th October 2019) available from: http://www.icmr.nic.in/guidelines/ICMR_Ethical_Guidelines_2017.pdf*

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