Title: Reviewing proposals involving vulnerable populations

SOP Code: KIMS/SOP-20/V3

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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 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 are responsible for ensuring that IHEC 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 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, 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, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent.

4.2 Mandate

An audio-video recording of the informed consent process in case of vulnerable subjects in clinical trials of New Chemical Entity or New Molecular Entity including procedure of providing information to the subject and his understanding on such consent, shall be maintained by the investigator for record. In case of clinical trial of anti-HIV and anti-leprosy drugs, only audio recording of the informed consent process of individual subject including the procedure of providing information to the subject and his understanding on such consent shall be maintained by the investigator for record. (The new CT rules 2019)

5. Detailed instructions

5.1. Reviewing protocols with vulnerable participants

- The protocol should be reviewed as per KIMS/SOP-8A/V3. Additionally, the 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- KIMS/SOP-20/02). Also, should ensure that study conform to the institutional policy (Annexure 6 - KIMS/SOP-20/02).

5.2. Appointing Reviewers

The 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 as per the particular vulnerable group 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 as per this SOP and KIMS/SOP-08A/V3.

- The discussion will be documented in the minutes.
- The IHEC members will discuss the comments in the IHEC meeting and letter regarding approval/modification/ disapproval will be sent to the principal investigator.
- The 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, the participant will be re-consented.

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. Appropriate modifications should be made as per individual IHEC requirement

Annexure 1 *ANX-01KIMS/SOP-20/V3* – Checklist: Requirements for Research Involving Children

Annexure 2 *ANX-02/KIMS/SOP-20/V3* - Checklist: Requirements for Research Involving Pregnant Women & Fetuses

Annexure 3 *ANX-03/KIMS/SOP-20/V3*- Checklist: Research Involving Cognitively Impaired Adults Annexure 4 *ANX-04/KIMS/SOP-20/V3*- Checklist-Research Involving Students, Employees or Residents

Annexure 5 *ANX-05/KIMS/SOP-20/V3* – Checklist: Considerations for Genetic Research

Annexure 1: ANX-01/KIMS/SOP-20/V3

Checklist: Requirements for Research Involving Children

Name of Principal Investigator:

Study Title:

For the principal investigator		IHEC Office
RISK DETERMINATION	BENEFIT ASSESSMENT	IHEC ACTION
Minimal * ☐	Direct benefit	Approvable
☐	No direct benefit	
Greater than minimal risk ☐	Potential benefit to child	Approvable
Greater than minimal risk ☐	No direct 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 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?			
a) If yes: Is the inclusion of healthy children justified?			
Are the studies conducted on animals and adults appropriate and justified?			
a) 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?			
a) If Yes: Are conditions under which one of the parents may be considered: "not reasonably available" described?			
b) 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 assent of children over 7 and, where appropriate, honoring 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 IHEC member during consent procedures?			

Are special needs of adolescents such as counseling 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 _____

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Comments of Primary Reviewer:	
Primary Reviewer	Signature and Date

Checklist: Requirements for Research Involving Pregnant Women and Fetuses

Name of Principal Investigator:			
Study Title:			
When research involves pregnant women or fetuses			
	Yes	**No**	**NA**
Is the risk to the fetus not greater than minimal, or any risk to the fetus which is greater than minimal caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus?			
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 representative obtained in accordance with the informed consent provisions, unless altered or waived?			
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?			
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 fetus?			
If the response to any of the above is **NO**, the research should not be approved by the IHEC **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 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?			
A. Fetuses of uncertain viability	**Yes**	**No**	**NA**
1. 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? OR**			

The purpose of the **research** is development of important biomedical knowledge which cannot be obtained by other means. Will there be a risk to the fetus 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 representative obtained?			
B. Nonviable fetuses	**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 knowledge that cannot be obtained by other means; and			
4. 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	Signature and Date

Annexure 3: ANX-03/KIMS/SOP-20/V3

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 favorable 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 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 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	Signature and Date

Annexure 4: AX 04/SOP-20/V3

Checklist: Research Involving Students, Employees or Residents

Name of Principal Investigator:

Study Title:

Participants who are students, employees or residents require special considerations.

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: ANX-05/KIMS/SOP-20/V3

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 genetic counseling being offered?		

Signature of Principal Investigator: _____ Date _____

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Comments of Primary Reviewer:	
Primary Reviewer	Signature and Date

KIMS Policy for Studies in Vulnerable Populations

Studies in vulnerable populations involve research that include children, pregnant & lactating women, and geriatric population. The detailed Guidelines for such studies are to be provided in the SOP of Institutional Ethics Committee.

1. As a general rule, pregnant or nursing women would not be participants of any clinical trial unless such trials are intended to protect or advance the health of pregnant or nursing women or foetus or nursing infants, and for which women who are not pregnant or nursing would not be suitable participants.
2. Children will not be involved in research that could be carried out equally well with adults.
3. Research in children shall be conducted only in settings in which the child and parent can obtain adequate medical and psychological support.
4. Geriatric patients can be only included in Phase III clinical trials (and in Phase II trials, at the Sponsor's option), and disease intended to be treated is characteristically a disease of aging, or the population to be treated is known to include substantial numbers of geriatric patients, or when there is specific reason to expect that conditions common in the elderly are likely to be encountered or they can be included, also the new drug is likely to alter the geriatric patient's response (with regard to safety or efficacy) compared with that of the non-geriatric patient.
5. Adequate justification is required for the involvement of subjects such as prisoners, students, subordinates, employees, and service personnel etc. who have reduced autonomy as research subjects.
6. Persons who are economically or socially disadvantaged and mentally challenged and mentally differently-abled persons, or those who have behavior disorder would not be included in any study except in exceptional circumstances as mentioned in the SOP of Institutional Ethics Committee.

7. Flow Chart