Title: Reviewing proposals involving vulnerable Populations.

SOP Code: **SOP 24/V1 Dated 18th February 2017**

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1. Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe procedures to review proposals involving vulnerable populations. The SOPs provide clear, unambiguous instructions so that the related activities of the Board are conducted in accordance with Indian laws and relevant, National and International Guidelines. It describes the requirements concerning review of research that involves groups that could be potentially vulnerable to coercion in regard to autonomy, and present conditions that may affect risk/benefit determinations or bearing unequal burden in research.

2. Scope

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

3. Responsibility

- It is the responsibility of the Secretariat of IEC to maintain up-to-date tools for review of research pertaining to vulnerable groups based on new and evolving applicable regulations and guidelines.
- IEC Chairperson/ Member Secretary is responsible for ensuring that IEC members are well versed in new and evolving regulations and guidelines pertaining to vulnerable populations, for selecting primary reviewers with appropriate expertise to conduct the reviews of such research, and for securing appropriate consulting expertise as needed for selected reviews.
- IEC member is responsible for conducting appropriate review of research planned for vulnerable populations, including an assessment of potential for coercion, in consultation with any appropriate experts and resources as described in this SOP

Secretariat of the Institutional Review Board will

- Maintain on file the update checklist (A-F) which conforms to applicable regulations and guidelines.
- Document review of risk assessment in IEC minutes for the protocols involving vulnerable population.
- Confirm that the complete informed consent and assent documents as relevant.

Chairperson / Member Secretary will:

Select appropriate primary reviewer(s).

IEC members will:

- Complete checklist during review of research with vulnerable populations and present recommendations at the convened meeting.

4. Flow Chart

No.	Activity	Responsibility
1	Reviewing the protocol with vulnerable population	Any member of IEC and designated reviewer, secretariat or administrative staff
2	Appoint one or more reviewers	Chairperson/ Member Secretary
3	Review the protocol	IEC members

5. Detailed instructions

Reviewing the protocol with vulnerable population

Vulnerable persons are those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests. Individuals whose willingness to volunteer in a research study 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 may also be considered vulnerable. 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 persons include patients with incurable diseases, people in nursing homes, unemployed or impoverished people, patients in emergency situations, ethnic minority groups, homeless people, nomads, refugees, minors, and those incapable of giving consent. This list may not be exhaustive as there may be circumstances in which other groups are considered vulnerable, women for example, in an orthodox patriarchical society.

The protocol should be reviewed keeping in mind the following points when it concerns research that involves groups that could be potentially vulnerable to coercion

- measure to protect autonomy,
- risk/benefit determinations with respect to the vulnerability
- bearing unequal burden in research.

Any member of the IEC or Secretariat who would be dealing with such protocols should be well versed with the potential harm or risk of such population participating in the study. The checklist for different vulnerable population is being provided in Annexure (A-F). Special justification is required for inviting vulnerable individuals to serve as research subjects and, if they are selected, the means of protecting their rights and welfare must be strictly applied.

Appoint the Reviewers

The 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. The reviewers should be familiar and trained in the concept of vulnerability and protections for participants with diminished autonomy.

Secretariat duties

- Provide a suitable checklist according to the subjects to be recruited in study to the investigator. Inform the investigator to download the appropriate application form and informed consent document/ assent form.
- Provide appropriate reference material or help reviewer locate such material related to vulnerable populations when specifically requested for, by a reviewing member

Reviewers responsibility

- IEC Members will review the protocol and the informed consent document or assent form.
- The reviewers comments will be discussed in the IEC meeting and the final comments will be sent to the PI.
- The discussion will be documented in the minutes.
- The member secretary will confirm that the IEC recommendations have been incorporated in the revised protocol and in the final draft of informed consent document or assent form.

Approval of the protocol

- The final version of the protocol will be approved by the board with the appropriate checklist as given in annexure (1-5).
- Wherever necessary the IEC approval should state that if in future the vulnerability status of the participants changes for e.g.; unconscious patient gaining consciousness, then the protocol and ICD should be amended and resubmitted to the IEC for reconsideration and approval Following which the participant should be re-consented and reconsidered for the same.

6. Glossary

SOP (Standard Operating Procedure)	Detailed, written instructions, in a certain format, describing activities and actions undertaken by the IEC to achieve uniformity of the performance of a specific function. The aim of the SOPs and their accompanying checklists and forms is to simplify the functioning, whilst maintaining high standards of Good Clinical Practice.
IEC members	Individuals serving as regular members of the Institutional Review Board. The Committee has been constituted in accordance with the EC membership requirements set forth in Schedule Y (20th January 2005)
Vulnerable population	Vulnerable persons are those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests.
Children	Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.
Assent	Assent means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.
	Pregnancy encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any

Pregnant women	of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.
Fetus	Fetus means the product of conception from implantation until delivery.
Viable fetus	Viable, as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.
Non viable fetus	Nonviable neonate means a neonate after delivery that, although living, is not viable.
Neonate	Neonate means a newborn.
Mentally impaired persons	Mentally incapable to give consent due to the situation /condition
Situational vulnerability	Disasters create vulnerable persons and groups in society, particularly so in disadvantaged communities,
Harm	is a negative safety or health consequence; any detrimental effect of a significant nature
Risk	"chance"/probability that harm can occur

7. References

1] Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants (Geneva 2011) - *www.who.int/...guideline.../operational-guidelines-ethics-biomedical-...* (last accessed 31st August 2013)

[2] International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996. *http://www.ich.org/LOB/media/MEDIA482.pdf* (last accessed 31st August 2013)

[3] ICMR's Ethical Guidelines for Biomedical research on Human Participants, ICMR (2006) - *http://www.icmr.nic.in/ethical_guidelines.pdf* (last accessed 31st August 2013)

[4] Schedule Y (Drugs and Cosmetic Act 1940; amendment 20th January 2005) *http://www.cdsco.nic.in/html/Schedule-Y%20(Amended%20Version-2005)%20original.htm* (last accessed 31st August 2013)

[5] Council for International Organizations of Medical Sciences (CIOMS) Guidelines *www.cioms.ch/publications/layout_guide2002.pdf* (last accessed 31st August 2013)

[6] Good Clinical Practices for Clinical Research in India *http://cdsco.nic.in/html/GCP.htm* (last accessed 31st August 2013)

[7] World Medical Association Declaration of Helsinki, *http:// www.wma.net/en/30publications/10policies/b3/* (last accessed 31st August 2013)

[8] ICMR-DBT Guidelines for Stem Cell Research 2012 (Draft), icmr.nic.in/*stem_cell_guidelines.pdf* (last accessed 31st August 2013)

[9] *http://www.mmcri.org/home/webSubContent.php?subCatID=4&catID=2&headType=IEC&catLevel=subCat* (last accessed 31st August 2013)

8. Annexure

Annexure 1	*AX 01/SOP 24/V1*	Checklist – Requirements for Research Involving Children
Annexure 2	AX 02/SOP 24/V1	Checklist – Requirements for Research Involving Pregnant Women & Fetuses
Annexure 3	AX 03/SOP 24/V1	Checklist- Research Involving Cognitively Impaired Adults
Annexure 4	AX 04/SOP 24/V1	Checklist-Research Involving Students, Employees or Residents
Annexure 5	AX 05/SOP 24/V1	Checklist- Considerations for Genetic Research

Annexure 1

AX 01/SOP 24/V1

Checklist –Requirements for Research Involving Children

Investigator:_____ IEC :

Study Title:_____

For the principal investigator		IEC Office
RISK DETERMINATION	BENEFIT ASSESSMENT	IEC ACTION
☐ Minimal *	☐ Direct benefit	Approvable
	☐ No direct benefit	
☐ Greater than minimal risk	☐ Potential to child	Approvable
☐ Greater than minimal risk	☐ No direct benefit to individual offer general knowledge about the child's condition or disorder.	Approvable case –by-case **

* 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.

** Risk may not be more than a minor increase over minimal risk, consent of both parents is required under normal circumstances.

	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 normal volunteers?	☐	☐	☐
If yes: Is the inclusion of normal volunteers 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 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 subjects’ privacy and the confidentially 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 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 a. which has implications for other family member ?(for example, genetic risk , HIV infection , Hepatitis C)	☐	☐	☐
If Yes: Are there adequate mechanisms in place to deal with other members of the family?	☐	☐	☐
Are parents be required to be present during the conduct of the research? (Are proposed subjects to be very young? Are the procedures involved painful? Must the subject stay overnight in the hospital when they otherwise would not have to?)	☐	☐	☐

- Approval to proceed with this category of research must be made by the Administrator of the IEC, with input from selected experts

Signature of Principal Investigator:_____Date _____

IEC Office use only	
Comments:	
Primary Reviewer Signature & Date	

Annexure 2

AX 02/SOP 24/V1

Checklist – Requirements for Research Involving Pregnant Women & Fetuses

Investigator: ***IEC #:***

Study Title:

SECTION 1

☐ **THIS RESEARCH INVOLVES PREGNANT WOMEN OR FETUSES PRIOR TO DELIVERY**

	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 fetuses;	☐	☐	☐
The risk to the fetus is not greater than minimal, or any risk to the fetus which is greater than minimal is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus;	☐	☐	☐
Any risk is the least possible for achieving the objectives of the research;	☐	☐	☐
The woman's consent or the consent of her legally authorized representative is obtained in accord with the informed consent provisions, unless altered or waived.	☐	☐	☐

The woman or her legally authorized representative, as appropriate, is fully informed regarding the reasonably foreseeable impact of the research on the fetus or resultant child;	☐	☐	☐
No inducements, monetary or otherwise, will be offered to terminate a pregnancy;	☐	☐	☐
Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and	☐	☐	☐
Individuals engaged in the research will have no part in determining the viability of a fetus.	☐	☐	☐

If the response to any of the above is No, the research is not approvable by the IEC at this time. See section 3

SECTION 2

☐ **THIS RESEARCH INVOLVES FETUSES AFTER DELIVERY**

	Yes	No	NA
1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to fetuses	☐	☐	☐
2. The individual(s) providing consent is fully informed regarding the reasonably foreseeable impact of the **research** on the fetus or resultant child;	☐	☐	☐
3. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;	☐	☐	☐
4. Individuals engaged in the **research** will have no part in any decisions as to the timing, method, or procedures used to terminate pregnancy;	☐	☐	☐
5. Individuals engaged in the **research** will have no part in determining the viability of a fetus.	☐	☐	☐

AND

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 any risk is the least possible for achieving the objectives of the **research;**	☐	☐	☐
OR			
The purpose of the **research** is the development of important biomedical knowledge which cannot be obtained by other means and there will be no risk to the fetus resulting from the **research**;	☐	☐	☐

2. The legally effective informed consent of either parent of the fetus 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 is obtained.	☐	☐	☐

And/or

B. Nonviable fetuses	Yes	No	NA
1. Vital functions of the fetus will not be artificially maintained;	☐	☐	☐
2. There will be no risk to the fetus 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 fetus 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 is not approvable by the IEC at this time. See section 3.

SECTION 3

THIS RESEARCH CAN BE CONDUCTED ONLY AFTER:

(a) The IEC finds that 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 or fetuses **and,**

(b) The secretary, after consultation with a panel of experts in pertinent disciplines (for examples: science, medicine, ethics, law) to determine either:

(1) That the research in fact satisfies the conditions of Schedule Y , as applicable, or

(2) The following:

(i) 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 or fetuses;

(ii) The research will be conducted in accord in sound ethical principles; and

(iii) Informed consent will be obtained in accord with informed consent provisions of Schedule Y and other applicable subparts, unless altered or waived in accord.

Signature of Principal Investigator:_____Date _____

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Comments:	
Primary Reviewer Signature & Date	

Annexure 3

AX 03/SOP 24/V1

Checklist- Research Involving Cognitively Impaired Adults

- The purpose of this checklist is to provide support for IEC members or the Designated Reviewer when reviewing research involving cognitively impaired adults as subjects.
  1. For review using the expedited procedure this checklist is to be completed by the **Designated Reviewer** to document determinations required by the regulations and protocol specific findings justifying those determinations and retained.
  2. For review using the convened IEC is to document determinations required by the regulations and protocol specific findings justifying these determinations.

1. **Research Involving Cognitively Impaired Adults in which there is Anticipated Direct Benefit to the subject** (All items must be "Yes")		
☐ Yes	☐ No	One of the following is true (Check the box t-hat is true) ☐ The risk to the subjects is presented by an intervention or procedure that holds out prospect of direct benefit for the individual subject. ☐ More than minimal risk to subjects is

		presented by monitoring procedure that is likely to contribute to the subjects well – being.
☐ Yes	☐ No	The risk is justified by the anticipated benefit to the subjects.
☐ Yes	☐ No	The relation of anticipated benefit to the risk is at least as favourable to the subjects as that presented by available alternative approaches.
☐ Yes	☐ No	The proposed plan for the assessment of the capacity to consent is adequate.
☐ Yes	☐ No	Assent is required of: (One of the following must be **"Yes")** One of the following is true (**Check box that is true)** ☐ All Subjects ☐ All Subjects capable of being consulted. ☐ None of the subjects
☐ Yes	☐ No	The consent document includes a signature line for a legally authorized representative.

2.Research Involving Cognitively Impaired Adults in which there is No Anticipated Direct Benefit to the subject (All items must be "Yes")		
☐ Yes	☐ No	The proposed plan for the assessment of the capacity to consent is adequate.
☐ Yes	☐ No	The objectives of the trial cannot be met by means of study of subjects who can give consent personally.
☐ Yes	☐ No	The foreseeable risks to the subjects are low.
☐ Yes	☐ No	The negative impact on the subject's well-being is minimized and low.

☐ Yes	☐ No	The trial is not prohibited by law.
☐ Yes	☐ No	Subjects have a disease or condition for which the procedures in the research are intended.
☐ Yes	☐ No	Subjects will be particularly closely monitored.
☐ Yes	☐ No	Subjects will 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	Assent is required of (One of the following must be **"Yes")** One of the following is true **(Check box that is true**) ☐ All Subjects ☐ All Subjects capable of being consulted. ☐ None of the subjects
☐ Yes	☐ No	The consent document includes a signature line for a legally authorized representative.

Signature of Principal Investigator:_____Date _____

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Comments:	
Primary Reviewer Signature & Date	

Annexure 4

AX 04/SOP01/V1

Checklist-Research Involving Students, Employees or Residents

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

Does the employer or supervisor of the research subject need to be aware of the research project?	☐ No	☐ Yes
Is there a letter of support and/ or internal services checklist?	☐ No	☐ Yes

Have the subjects 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 subjects been minimized?	☐ No	☐ Yes
Have subjects been assured that participation is voluntary (no signs of coercion)?	☐ No	☐ Yes
Have subjects been assured that confidentiality will be protected or maintained?	☐ No	☐ Yes

Signature of Principal Investigator:_____Date _____

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Comments:	
Primary Reviewer Signature & Date	

Annexure 5

AX 05/SOP 24/V1

Checklist - Considerations for Genetic Research

Investigator: ***IEC #***

Study Title:

	Yes	No
1. Will the samples be made anonymous to maintain confidentiality? If yes, stop here	☐	☐
2. Has the investigator established clear guidelines for disclosure of information, including interim or inconclusive research result?	☐	☐
3. Has the appropriateness of the various strategies for recruiting subjects 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. Is genetic counseling being offered?	☐	☐

Signature of Principal Investigator:_____Date _____

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Comments:	
Primary Reviewer Signature & Date	