Title: Vulnerable Population

SOP Code: SOP/09/V1.3

Effective date : 07/11/2017

Table of Contents

The Declaration of Helsinki states that 'Medical research involving a underprivileged or vulnerable population or community is only justified if the research is responsive to the health needs and priorities of that population or community and if there is a reasonable likelihood that this population or community stands to benefit from the results of the research.'

1. Purpose

The purpose of this SOP is to describe how the IEC will ensure that the rights and interests of vulnerable population are safeguarded. The EC will ensure that individuals or communities included for research are selected in such a way that the burdens and benefits of the research are equally distributed.

2. Scope

This SOP applies to the process by which the EC will protect the rights and interests of vulnerable population. Additional protection will be ensured depending upon the risk of harm and the likelihood of benefit.

3. Responsibility

It is the responsibility of the EC members to identify study proposals including vulnerable population and ensure that these are considered for full board. The EC will ensure that measures for safeguarding rights and interests of vulnerable participants are mentioned in the face sheet, study proposal, Participant /Assent Information Sheet/ and informed consent/assent form. They have the responsibility to ensure that the vulnerable population is not exploited and they will guide the investigators to design protocols and describe the process of informed consent in such a manner that this will be done.

4. Flow chart

No.	Activity	Responsibility
1	Receive the submitted documents ↓	IEC Secretariat
2	Determine protocols including vulnerable population ↓	IEC members and Chairperson
3	Review of protocol by appropriate reviewes and assess whether their inclusion is justified ↓	IEC members and Chairperson
4	Ensure measures for protecting rights and interests of vulnerable population are described in the face sheet ↓	IEC members and Chairperson
5	Review the Participant /Assent Information Sheet/ and Informed Consent/Assent form	IEC members and Chairperson

5. Detailed instructions

5.1 Determine protocols including vulnerable population

Project proposals presented before the Ethics Committee Meeting which includes vulnerable population: It is the responsibility of the EC to see whether the inclusion of vulnerable populations in the study is justifiable or the population is just being exploited to generate

clinical data. In such cases, appropriate reviewers will assess the risk and ensure measures for protecting their rights. Review of risk assessment will be documented in IEC minutes.

5.2 Vulnerable groups: Effort may be made to ensure that individuals or communities invited for research be selected in such a way that the burdens and benefits of the research are equally distributed.

a. Research on genetics should not lead to racial inequalities;
b. Persons who are economically or socially disadvantaged should not be used to benefit those who are better off than them;
c. Rights and welfare of mentally challenged and mentally differently able persons who are incapable of giving informed consent or those with behavioural disorders must be protected. Appropriate proxy consent from the legal guardian should be taken after the person is well informed about the study, need for participation, risks and benefits involved and the privacy and confidentiality procedures. The entire consent process should be properly documented;
d. Adequate justification is required for the involvement of participants such as prisoners, students, subordinates, employees, service personnel etc. who have reduced autonomy as research participants, since the consent provided may be under duress or various other compelling reasons.
e. Persons who are terminally ill, have incurable disease and mental illness and cognitively impaired and physically disabled.
f. Pregnant and lactating women
g. Children (<18 years)
h. Tribal and marginalized communities
i. Refugee, migrants, homeless, persons or populations in conflict zones, riots areas or disaster situations;
j. Suffering from stigmatizing or rare diseases etc.

5.2.1 Consideration issues and protection of specific vulnerable groups:

i. *Children* :

Before undertaking research/trial in children the investigator must ensure that –

a. Children will not be involved in research that could be carried out equally well with adults;
b. The purpose of the research is to obtain knowledge relevant to health needs of children. For clinical evaluation of a new drug the study in children should always be carried out after the phase III clinical trials in adults. It can be studied earlier only if the drug has a therapeutic value in a primary disease of the children;
c. A parent or legal guardian of each child has given consent;
d. The assent of the child should be obtained to the extent of the child's capabilities such as in the case of mature minors from the age of seven years up to the age of 18 years.;
e. Research should be conducted in settings in which the child and parent can obtain adequate Medical and psychological support;
f. Interventions intended to provide direct diagnostic, therapeutic or preventive benefit for the individual child participant must be justified in relation to anticipated risks involved in the study and anticipated benefits to society;

g. The child's refusal to participate in research must always be respected unless there is no medically acceptable alternative to the therapy provided/ tested, provided the consent has been obtained from parents / guardian;
h. Interventions that are intended to provide therapeutic benefit are likely to be at least as advantageous to the individual child participant as any available alternative interventions;
i. The risk presented by interventions not intended to benefit the individual child participant is low when compared to the importance of the knowledge that is to be gained.

ii. Pregnant or nursing women:

Pregnant or nursing women should in no circumstances be the participant of any research unless the research carries no more than minimal risk to the fetus or nursing infant and the object of the research is to obtain new knowledge about the foetus, pregnancy and lactation.
As a general rule, pregnant or nursing women should not be participants of any clinical trial except such trials as are designed to protect or advance the health of pregnant or nursing women or foetuses or nursing infants, and for which women who are not pregnant or nursing would not be suitable participants.

a. The justification of participation of these women in clinical trials would be that they should not be deprived arbitrarily of the opportunity to benefit from investigations, drugs, vaccines or other agents that promise therapeutic or preventive benefits.
Example of such trials are,
- To test the efficacy and safety of a drug for reducing perinatal transmission of HIV infection from mother to child,
- Trials for detecting foetal abnormalities and for conditions associated with or aggravated by pregnancy etc.
- Women should not be encouraged to discontinue nursing for the sake of participation in research and in case she decides to do so, harm of cessation of breast-feeding to the nursing child should be properly assessed except in those studies where breast feeding is harmful to the infant. Compensation in terms of supplying supplementary food such as milk formula should be considered in such instances.

b. **Research related to termination of pregnancy:** Pregnant women who desire to undergo Medical Termination of Pregnancy (MTP) could be made participants for such research as per The Medical Termination of Pregnancy Act, GOI, 1971.

c. **Research related to pre-natal diagnostic techniques :** In pregnant women such research should be limited to detect the foetal abnormalities or genetic disorders as per the Prenatal Diagnostic Techniques (Regulation and Prevention of Misuse) Act, GOI, 1994 and not for sex determination of the foetus.

iii. An audio-video recording of the informed consent process in case of vulnerable participants in clinical trials of New Chemical Entity or New Molecular Entity including procedure providing information to the participants and his understanding of such consent, shall be maintained by the investigator for record.

6. Glossary

Vulnerability

- The Council for International Organizations of Medical Sciences **(CIOMS)** defines **vulnerability** as "Substantial incapacity to protect one's own interests owing to such impediments as lack of capability to give informed consent, lack of alternative means of obtaining medical care or other expensive necessities, or being a junior or subordinate member of a hierarchical group."
- **Vulnerable (research) participants:** 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. (WHO)

7. References

1. Ethical Guidelines for Biomedical Research on Human Participants , ICMR , 2006
2. E6 Good Clinical Practice: Consolidated Guidance, April 1996, ICH –GCP
3. WHO Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants , 2011
4. Training curriculum for ethics in clinical research - www.fhi.org
5. SOPs Ethics Committee for Research on Human Participants – Seth GS Medical College and KEM Hospital, Mumbai Reference: SOP-20 reviewing proposal involving vulnerable population
6. Order from Director General of Health Services (DGHS), Ministry of Health and Family Welfare, Office of Drugs Controller General (India), Gazette of Indian New Delhi, dated 31st July 2015 No.489.
7. National Ethical Guidelines for Medical and Health Research Involving Human participants, ICMR 2017

8. ANNEX

ANNEX 1	Document history	AF/EC/01/09/V1.3
ANNEX 2	Checklist Requirements for research involving Children	AF/EC/02/09/V1.3
ANNEX 3	Checklist Requirements for research involving pregnant women and foetuses	AF/EC/03/09/V1.3
ANNEX 4	Checklist Requirements for research involving cognitively impaired	AF/EC/04/09/V1.3
ANNEX 5	Checklist Requirements for research involving employees, students or residents	AF/EC/05/09/V1.3
ANNEX 6	Checklist- Consideration for Genetic Research	AF/EC/06/09/V1.3
ANNEX 7	Requirements for research involving vulnerable population	AF/EC/07/09/V1.3

ANNEX 1 AF/EC/01/09/V1.3

Document history

Author	Version	Date	Description of the Change
Dr. Ragini Kulkarni	Version 1.1	24th September 2014	Flow Chart improved on Page 3
Dr. Ragini Kulkarni	Version 1.2	4th March 2016	Inclusion of the paragraph under 5.2.1, bullet iii - regarding AV consent in case of vulnerable participants
Dr. Ragini Kulkarni	Version 1.3	7th November 2017	Pg. 4, 5.2 Point e, modified Pg. 4, 5.2 New points f to j added Pg. 4, 5.2.1(i) c 'Proxy' word deleted Pg. 5, Point iii, 'subjects' replaced with 'participants' Pg. 6, Reference 5 modified, Reference 7 added Annexure 2 to 7, added checklists for Different types of Vulnerable populations

Annexure 2 AF/EC/02/09/V1.3

Checklist-Requirements for research involving children

	Yes	No	NA
Are safe guards in place to minimize these risks?			
Is permission of both parents necessary?			
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, honouring their dissent?			
Are provisions made to protect participants' privacy and the confidentially of information regarding procedures?			
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?			

Comments	
Primary Reviewer name, Signature and Date	

Annexure 3 AF/EC/03/09/V1.3

Checklist- Requirements for research involving pregnant women and foetuses

☐ The research involves pregnant women or foetus prior to delivery	Refer section 1
☐ The research involves foetuses after delivery	Refer section 2

Section 1	**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;			
The risk to the foetus is not greater than minimal, or any risk to the foetus 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 foetus;			
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 foetus			
No inducements, monetary or otherwise, will be offered to terminate a pregnancy;			
Women's participation in the research will not have an effect on the decisions by investigator with respect to the timing, method or procedures used to terminate a pregnancy; and			
The decision of investigator determining the viability of a foetus will not have an effect if the women participates in the research			

Section 2	**Yes**	**No**	**NA**
Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to foetuses			
The individual(s) providing consent is fully informed regarding the reasonably foreseeable impact of the research on the foetus			

No inducements, monetary or otherwise, will be offered to terminate a pregnancy;			
Women's participation in the research will not have an effect on the decisions by investigator with respect to the timing, method or procedures used to terminate a pregnancy;			
The decision of investigator determining the viability of a foetus will not have an effect if the women participates in the research			
AND			
A. Fetuses of uncertain viability	Yes	No	NA
Does the research hold out the prospect of enhancing the probability of survival of the particular foetus 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 foetus resulting from the research;			
The legally effective informed consent of either parent of the foetus 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 foetuses	Yes	No	NA
Vital functions of the foetus will not be artificially maintained;			
There will be no risk to the foetus resulting from the research;			
The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and			
The legally effective informed consent of both parents of the foetus 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 foetus 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 foetus will not suffice to meet the requirements of this paragraph			

Comments	
Primary Reviewer name, Signature and Date	

Annexure 4 AF/EC/04/09/V1.3

Checklist- Requirements for research involving cognitively impaired

1.Research Involving Cognitively Impaired Adults in which there is Anticipated Direct Benefit to the participants

One of the following is true (Check the box that is true)

☐The risk to the participants is presented by an intervention or procedure that holds out prospect of direct benefit for the participants.

☐More than minimal risk to participants is presented by monitoring procedure that is likely to contribute to the participants well being.

	Yes	No	NA
The risk is justified by the anticipated benefit to the participants			
The relation of anticipated benefit to the risk is at least as favourable to the participants as that presented by available alternative approaches			
The proposed plan for the assessment of the capacity to consent is adequate.			
Assent is required of: (One of the following must be "Yes") ☐All participants ☐All participants capable of being consulted. ☐None of the participants			
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 participants

	Yes	**No**	**NA**
The proposed plan for the assessment of the capacity to consent is adequate			
The objectives of the trial cannot be met by means of study of participants who can give consent personally			
The foreseeable risks to the participants are low			
The negative impact on the participants well-being is minimized and low.			
The trial is not prohibited by law.			
Participants have a disease or condition for which the procedures in the research are intended.			
Participants will be particularly closely monitored.			
Participants will be withdrawn if they appear to be unduly distressed.			
The proposed plan for the assessment of the capacity to consent is adequate.			
Assent is required of (One of the following must be **"Yes")** ☐All participants ☐All participants capable of being consulted. ☐None of the participants			
The consent document includes a signature line for a legally			

authorized representative.			

Comments	
Primary Reviewer name, Signature and Date	

Annexure 5 AF/EC/05/09/V1.3

Checklist- Requirements for research involving employees, students, residents or any other vulnerable

	Yes	No	NA
Does the employer or supervisor of the research participant need to be aware of the research project?			
Have the participants been assured that their status (education, employment, and/or promotion) will not be affected by any decision to participate or not?			
Have the risks to participants been minimized?			
Have participants been assured that participation is voluntary (no signs of coercion)?			
Have participants been assured that confidentiality will be protected or maintained?			

Comments	
Primary Reviewer name, Signature and Date	

Annexure 6 AF/EC/06/09/V1.3

Checklist- Consideration for Genetic Research

	Yes	No	NA
Will the samples be made anonymous to maintain confidentiality?			
Has the investigator established clear guidelines for disclosure of information, including interim or inconclusive research result?			
Has the appropriateness of the various strategies for recruiting participants and their family members been considered?			
Does the proposed study population comprise family members?			
Will family members be implicated in the studies without consent?			
Will the samples be destroyed in the future?			
Is genetic counselling being offered?			

Comments	
Primary Reviewer name, Signature and Date	

Annexure 7 AF/EC/07/09/V1.3

Checklist- Requirements for Research involving Vulnerable Population

Investigator:_____ IEC:

Study Title: _____

Vulnerable population:_____

For IEC		
Risk Determination	**Benefit Assessment**	**IEC action**
☐ Less than Minimal Risk*	☐ Direct benefit ☐ No direct benefit	Approvable
☐ Minimal Risk**	☐ Direct benefit ☐ No direct benefit	Approvable
☐ Low Risk*** (Minor increase over minimal risk)	☐ Direct benefit ☐ No direct benefit	Approvable
☐ High Risk**** (more than minimal risk)	☐ Direct benefit ☐ No direct benefit	Approvable

***Less than Minimal risk**: Probability of harm or discomfort anticipated in the research is nil or not expected. For example, research on anonymous or non- identified data/ samples, data available in the public domain, meta-analysis etc.

**** Minimal risk**: Probability of harm or discomfort anticipated in the research is not greater than that ordinarily encountered in routine daily life activities of an average healthy individual or general population or during the performance of routine tests where occurrence of serious harm or an adverse event (AE) is unlikely e.g. research involving routine questioning or history taking, obtaining body fluids without invasive intervention, physical examination or chest X-ray etc.

***** Low risk**: (minor increase over minimal risk) Increment in probability of harm or discomfort is only a little more than the minimal risk threshold. This may present in situations such as routine research on children and adolescents; research on persons incapable of giving consent; delaying or withholding a proven intervention or standard of care in a control or placebo group during randomized trials; use of minimally invasive procedures that might cause no more than brief pain or tenderness, small bruises or scars, or very slight, temporary distress, such as drawing a small sample of blood for testing; trying a new diagnostic technique in pregnant and breastfeeding women, etc. Such research should have a social value. Use of personal identifiable data in research also imposes indirect risks. Social risks, psychological harm and discomfort may also fall in this category.

****** High risk**: (more than minimal risk) Probability of harm or discomfort anticipated in the research is invasive and greater than minimal risk. Examples include research involving any interventional study using a drug, device or invasive procedure such as lumbar puncture, lung or liver biopsy, endoscopic procedure, intravenous sedation for diagnostic procedures.