Title: Reviewing proposals involving vulnerable populations

SOP Code: SOP19/v2

Effective Date: 01/08/2016

Prepared by:

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1. Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe the requirements and process of review of research protocols involving participants from vulnerable populations.

2. Scope

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

3. Responsibility

3.1 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.

3.2 The YUEC 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 programs.

3.3 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.

3.4 YUEC 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: For the purpose of this SOP, vulnerable subjects are defined as 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[1].

4.2 Mandate: Gazette notification (GoI) dated 31st July 2016 has mandated audio-visual recording of informed consent process in case of vulnerable participants in clinical trials of new chemical entity/new molecular entity[2].

5. Detailed instructions

5.1 Reviewing protocols involving vulnerable populations:

5.1.1 The protocol should be reviewed as per SOP7A/v2. Additionally, the protocol should be reviewed to assess if the following questions 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 measures to protect the autonomy of the vulnerable population been described

5.1.2 YUEC members dealing with such protocols should be well versed with the potential harm or risk of such population participating in the study.

5.1.3 The review must address all points in the checklists for different vulnerable populations (Annexures 1-5 of SOP19/v2).

[1] http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf accessed on 12 July 2016 at 1645 hours.

[2] http://www.ferci.org/wp-content/uploads/2014/07/Gazette-Notification-31-July-2015-AV-consent.pdf accessed on 12 July 2016 at 1722 hours.

5.2 Appointing reviewers: The Member Secretary/Chairperson will appoint two or more members of the YUEC 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 Responsibilities of the Secretariat:

5.3.1 All research studies involving vulnerable populations, whether regulated clinical trials or not, exposing the participants to more than minimal risk, will be subjected to a full review.

5.3.2 The Secretariat should provide an appropriate checklist to the investigator, depending on the type of participant being recruited for the study.

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

5.3.4 Research protocols involving vulnerable populations, exposing the participants to minimal or less than minimal risk, can be considered for 'expedited review' based on the judgment of the Member-Secretary/Jt Secretary.

5.4 Responsibilities of reviewers:

5.4.1 YUEC members will review the protocol and the informed consent document or assent form as per this SOP and SOP 07A/v2.

5.4.2 If kept for 'full review', the YUEC members will discuss the comments in the YUEC meeting and the discussion will be documented in the minutes.

5.5 Approval of the protocol:

5.5.1 The final version of the protocol (with amendments), if initially categorized as 'full review' will be once more kept for full review and approved at a subsequent YUEC meeting, except when the YUEC expressly authorizes the Member-Secretary, in the minutes of the initial discussion itself, to ascertain the amendments are to the satisfaction of the YUEC and issue ethical clearance.

5.5.2 Whenever so empowered, the Member-Secretary will ensure that recommendations have been incorporated in the revised protocol and protocol related documents before

issuing ethical clearance.

5.5.2 Wherever necessary the YUEC 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

Annexure 1: Ann01/SOP19/v2 - Checklist: Requirements for Research Involving Children

Annexure 2: Ann02/SOP19/v2 - Checklist: Requirements for Research Involving Pregnant Women & Fetuses

Annexure 3: Ann03/SOP19/v2 - Checklist: Research Involving Cognitively Impaired Adults

Annexure 4: Ann04/SOP19/v2 - Checklist-Research Involving Students, Employees or Residents

Annexure 5: Ann05/SOP19/v2 - Checklist: Considerations for Genetic Research

Annexure 1: Ann01/SOP19/v2

Checklist: Requirements for Research Involving Children (minors below the age of 18 years)

Study Title:

Name of the Principal Investigator:

No.	Checklist item for the PI to fill before submission (information provided here should also clearly and unambiguously reflect in the protocol)	Y	N	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?			
4A. If yes:				
4Ai	Is the inclusion of healthy children justified?			
4Aii	Are studies conducted on animals and/or adults appropriate and justified?			
4B. If no:				
4Bi	Is the lack of studies conducted on animals and/or adults justified?			
5	Will older children be enrolled before younger ones?			
6	Is permission of both parents necessary?			
If yes:				
6A	Are conditions under which one of the parents may be considered: "not reasonably available" described?			
6B	Are the conditions acceptable?			
7	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?			
8	Are provisions made to obtain the assent of children over 12 years, and where appropriate, honoring their dissent?			
9	Are provisions made to protect participants' privacy and the confidentiality of information regarding procedures?			
10	Are there special problems that call for the presence of a monitor or IEC member during consent procedures?			
11	Are special needs of adolescents such as counseling and confidentiality accounted for in the research design?			
12	Are there any special problems such as confidentiality and reporting that might arise in sensitive research about child abuse or sexual practices of teenagers?			
13	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:				
13A	Are there adequate mechanisms in place to deal with other members of the family?			

14	Are parents required to be present during the conduct of the research?			

For the Principal Investigator *(tick whichever is applicable in the risk-benefit columns)*		**For the YUEC Secretariat** *(this column for YUEC; circle whatever is applicable)*
Risk determination	**Benefit assessment**	**YUEC Action**
Minimal risk*	Direct benefit	Approvable
	No direct benefit	Approvable
Greater than minimal risk	Potential benefit to participant	Approvable
	No direct benefit; or offers new knowledge about the condition being investigated	Case-based approval on merits

* *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*

** *Consent of both parents (and assent) may be needed as applicable*

Signature of the Principal Investigator:

Date:

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

Annexure 2: Ann02/SOP19/v2

Checklist: Requirements for Research Involving Pregnant Women & Fetuses

Name of the Principal Investigator :

Study Title:

When research involves pregnant women or fetuses:

Sl.No.	**Checklist item**	**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 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?			
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 YUEC.

When the research involves neonates after delivery:

Sl No	Checklist item	Y	N	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?			

Fetus of uncertain viability:

Sl No	Checklist item	Y	N	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?			

Non-viable fetus:

Sl No	Checklist item	Y	N	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			
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 YUEC.

<u>This type of research can be conducted only after YUEC determines 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 the Principal Investigator:

Date:

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

Annexure 3: Ann03/SOP19/v2

Checklist: Research Involving Cognitively Impaired Adults

Name of the Principal Investigator :

Study title:

1. **Research Involving Cognitively Impaired Adults in which there is anticipated direct benefit to the participant**
   (All items should be answered 'yes' and the protocol should reflect these)

Sl No	Checklist item	Y	N	NA
1	Is the recruitment of participants justified considering the rationale and objectives of the study?			
2	Is the risk justified by the anticipated benefit to the participants?			
3	Is the relation of anticipated benefit to the risk at least as favorable to the participants as that presented by available alternative approaches.			
4	Will the participants be withdrawn if they appear to be unduly distressed?			
5	Is the proposed plan for the assessment of the capacity to consent adequate?			
6	Will consent be taken from participants capable of being consulted?			
7	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 answered 'yes' and the same should reflect in the protocol)

Sl No	Checklist item	Y	N	NA
1	Is the recruitment of participants justified considering the rationale and objectives of the study?			
2	Are the foreseeable risks to the participants low?			
3	Is the negative impact on the participant's well-being minimized and low?			
4	Will the participants be closely monitored?			
5	Will the participants be withdrawn if they appear to be unduly distressed?			
6	Is the proposed plan for the assessment of the capacity to consent adequate?			
7	Will consent be taken from participants capable of being consulted?			

8	Does the consent document include provision for a legally authorized representative in case participants are not capable of being consulted?			

Signature of the Principal Investigator:
Date:

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Comments of Primary Reviewer	
Primary Reviewer Signature and Date	

Annexure 4: Ann04/SOP19/v2

Checklist-Research Involving Students, Employees or Residents

Name of the Principal Investigator:

Study title:

Sl No	**Checklist item**	**Y**	**N**	**NA**
1	Have the participants been assured that their status (education, employment and/or promotion) will not be affected by any decision to participate or not?			
2	Have the risks to participants been minimized?			
3	Have participants been assured that participation is voluntary (no signs of coercion)?			
4	Have participants been assured that privacy and confidentiality will be protected?			

All items must be marked 'yes' and the same should reflect in the protocol

Signature of Principal Investigator
Date:

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Comments of Primary Reviewer	
Primary Reviewer Signature and Date	

Annexure 5: Ann05/SOP19/v2

Checklist: Considerations for Genetic Research

Name of the Principal Investigator

Study Title:

Sl No	Checklist item	Y	N	NA
1	Will the samples be made anonymous to maintain confidentiality?			
2	Will the results be disclosed to the participant or legally authorized representative? 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 the Principal Investigator:

Date:

YUEC Office use only	
Comments of Primary Reviewer	
Primary Reviewer Signature and Date	

7. Flow Chart

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