# Institutional Review Board, Tata Memorial Centre (IRB,TMC)

## Title: Reviewing Research Protocols Involving Vulnerable Populations

## SOP Code: SOP 17/V1 Date : 06/03/2013 Pages: 1 to 17

## 17.1 Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe procedures to review research protocol 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.

## 17.2 Scope

- This SOP applies to all policies and procedures of review and assessment applied to all research dealing with vulnerable population that require additional consideration or protection, submitted and approved by the IRB.

- 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.

"Vulnerable" or "special" classes of subjects include as listed below

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, or terminally ill cancer patients.

- pregnant women, human fetuses and neonates,
- prisoners,
- children,
- cognitively impaired persons
- students and employees, sub-ordinates (Ref App1/V1)

- minorities (as defined by national constitution and / or socio-economically backward, refugees and such others.
- economically and/or educationally disadvantaged
- AIDS/HIV+ subjects.
- Terminally ill Subjects
- Geriatic population

### 17.3 Categorization of protocols

Vulnerable population will be subjected to full board Initial review (SOP 4aV1). Research involving vulnerable populations is not eligible for expedited review or exemption from review.

### 17.4 Review Process

- The IRB evaluates whether additional safeguards have been included in the study to protect the rights and welfare of vulnerable participants.

- The IRB requires at least one or more individuals who are knowledgeable about or have experience in working with these participants are part of the review process.

- New study submissions, amendment and continuing review applications involving vulnerable populations (except prisoners, which should be reviewed by the full board) may be reviewed by the convened board or by expedited review, as decided during initial review and as per SOP 4b.

The research protocol involving Vulnerable population will be reviewed according to current requirement and guidelines. The decisions are arrived at using the approved checklist for reviewers (Refer Annexure A-F).

If the research includes a vulnerable population that is not covered in the above list or there are no national or international guidelines for ensuring protections. IRB will evaluate the research proposal to ensure that precautions are taken to protect the participants.

The protocol should be reviewed keeping in mind the following points:

- measures to protect autonomy,
- risk/benefit determinations with respect to the vulnerability
- whether vulnerable subjects are bearing unequal burden in research.

Member of the IRB who would be reviewing 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 provided in Annexure (A-F) should be used. 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 adhered to.

The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations. The central issue for the IRB to consider is whether the potential subject's ability to exercise free choice is limited in some way.

## 17.5 Responsibility

**The IRB Secretariat** is responsible for receiving, verifying, and managing the hard copies of the received research protocols pertaining to vulnerable groups based on new and evolving applicable regulations and guidelines as per the checklist.

The Secretariat should create a study specific file, distribute the packages and study assessment forms to the IRB members for review with the updated checklist (A-F), and communicate the review results to the investigators.

- It is the responsibility of the IRB Secretariat to maintain up-to-date tools (e.g. checklist) for review of research pertaining to vulnerable groups based on new and evolving applicable national and international regulations and guidelines.
- Maintain file for update-checklist (A-F) which conforms to recent / current applicable regulations and guidelines.

**The Member Secretary** will assign two or more members of the IRB 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.

**IRB Chairperson/ Member Secretary** is responsible for ensuring that IRB members are well versed in new and evolving regulations and guidelines pertaining to vulnerable populations through regular training programmes, 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.

IRB members are responsible for receiving, verifying, and reviewing the research protocols pertaining to vulnerable populations using study assessment form and ckecklist (Refer SOP17, Annexure A-F).

IRB 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

IRB Members will review the protocol and the informed consent document or assent form (Refer SOP 4a.5.4 and Appendices 7/V1).

The suggestions that are agreed upon by the IRB members present at the meeting will be discussed.

### 17.6 IRB Meeting

- The details of review procedures and communication of decision is described in detail in SOP05/V1
- Document review of risk assessment in IRB minutes for the protocols involving vulnerable population.
- IRB Member Secretary will minute the discussions in the respective month minutes

### Reference

[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 4 February 2013)

[2] International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996. *http://www.ich.org/LOB/media/MEDIA482.pdf* (last accessed 24 March 2008)

[3] ICMR's Ethical Guidelines for Biomedical research on Human Participants, ICMR (2006) - *http://www.icmr.nic.in/ethical_guidelines.pdf* (last accessed 24 March 2008)

[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 24 March 2008)

[5] Council for International Organizations of Medical Sciences (CIOMS) Guidelines *www.cioms.ch/publications/layout_guide2002.pdf* (last accessed 24 March 2008)

[6] Good Clinical Practices for Clinical Research in India *http://cdsco.nic.in/html/GCP.htm* (last accessed 24 March 2008)

[7] World Medical Association Declaration of Helsinki, *http:// www.wma.net/en/30publications/10policies/b3/* (last accessed 24 March 2008)

[8] ICMR-DBT Guidelines for Stem Cell Research 2012 (Draft), *icmr.nic.in/stem_cell_guidelines.pdf* (last accessed 4 February 2013)

[9] Code of Federal Regulations, http://www.hhs.gov / ohrp / humansubjects / guidance / 45cfr46.html

## Annexures

| | | |
|---|---|---|
| Annexure 1 | *AX 01/SOP 17/V1* | Checklist – Requirements for Research Involving Children |
| Annexure 2 | AX 02/SOP 17/V1 | Checklist – Requirements for Research Involving Pregnant Women & Fetuses |
| Annexure 3 | AX 03/SOP 17/V1 | Checklist- Research Involving Cognitively Impaired Adults |
| Annexure 4 | AX 04/SOP 17/V1 | Checklist-Research Involving Students, Employees or Residents |
| Annexure 5 | AX 05/SOP 17/V1 | Checklist- Considerations for Genetic Research |

**Annexure 1**

*AX 01/SOP 17/V1*

**Checklist –Requirements for Research Involving Children**

Investigator IRB :

Study Title:

| RISK DETERMINATION | BENEFIT ASSEMENT | IRB ACTION |
|---|---|---|
| □ Minimal (i) | With or without direct benefit | Approvable |
| □ 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 (ii) |

(i) Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

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

(iii) Approval to proceed with this category of research must be made by the Administrator of the IRB with input from selected experts

| | Yes | No | NA |
|---|---|---|---|
| Does the research pose greater than minimal risk to children? | □ | □ | □ |
| If yes: Are convincing scientific and ethical justification given ? | □ | □ | □ |
| If yes: Are adequate safeguard in place to minimize these risks ? | □ | □ | □ |
| Does the study involve normal volunteers? | □ | □ | □ |
| If yes: Is the inclusion of normal volunteers justified? | □ | □ | □ |

| | | | |
|---|---|---|---|
| Have appropriate studies been conducted on animals and adults justified? | ☐ | ☐ | ☐ |
| If No: Is the lack of appropriate 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 IRB 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 adequate mechanisms in place to deal with other members of the family ? | ☐ | ☐ | ☐ |
| Should 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 subject stay overnight in the hospital when they otherwise would not have to? ) | ☐ | ☐ | ☐ |

Comments :

_____

Primary Reviewer Date

**Annexure 2**

*AX 02/SOP 17/V1*

**Checklist – Requirements for Research Involving Pregnant Women & Fetuses**

***Investigator:*** ***IRB #:***
***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 in accord with 45 CFR | ☐ | ☐ | ☐ |
| 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; | ☐ | ☐ | ☐ |
| If the research involves children as defined in 45 CFR 46.402(a) who are pregnant, assent and permission will be obtained in accord with the provisions of subpart D of that part; | ☐ | ☐ | ☐ |
| 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 IRB 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 in accord with the subpart A of 45 CFR 46, except that the waiver and alteration provisions of and (d) 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 IRB at this time. See section 3.

**SECTION 3**
**THIS RESEARCH CAN BE CONDUCTED ONLY AFTER:**

(a) The IRB 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 45 CRF , 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 45CFR 46 subpart A and other applicable subparts, unless altered or waived in accord with 45 CFR or (d).

**Comments:**

**Primary Reviewer** **Date**

**Annexure 3**

*AX 03/SOP 17/V1*

**Checklist- Research Involving Cognitively Impaired Adults**

- The purpose of this checklist is to provide support for IRB 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 IRB 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 that is true)<br>☐ The risk to the subjects is presented by an intervention or procedure that holds out prospect of direct benefit for the individual subject.<br>☐ 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")**<br>One of the following is true (**Check box that is true)**<br>□ All Subjects<br>□ All Subjects capable of being consulted.<br>□ 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")**<br>One of the following is true **(Check box that is true**)<br>□ All Subjects<br>□ All Subjects capable of being consulted.<br>□ None of the subjects |
| □ Yes | □ No | The consent document includes a signature line for a legally authorized representative. |

**Annexure 4**

*AX 04/SOP17/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 |

**Annexure 5**

*AX 05/SOP 17/V1*

**Checklist - Considerations for Genetic Research**

***Investigator:***
***IRB#***
***Study Title:***

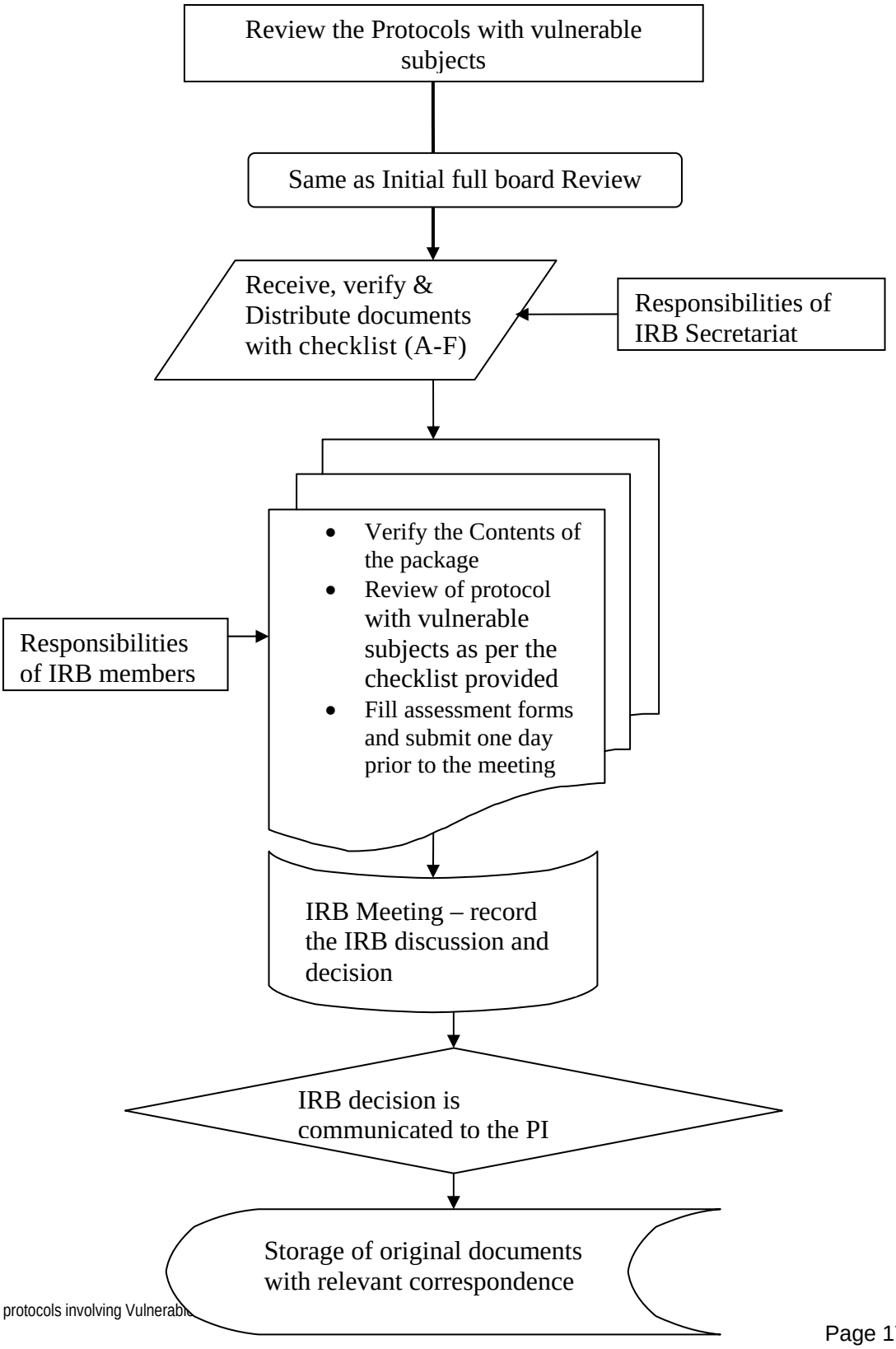
| | Yes | No |
|---|---|---|
| 1. Will the samples be made anonymous to maintain confidentiality? If yes, stop here | ☐ | ☐ |
| 2. Has the investigator established clear guidelines for disclosure of information, including interim or inconclusive research result? | ☐ | ☐ |
| 3. Has the appropriateness 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? | ☐ | ☐ |

***Comments:***

_____ _____

Primary Reviewer Date

# Flow Chart


Review the Protocols with vulnerable subjects
Same as Initial full board Review
Receive, verify & Distribute documents with checklist (A-F)
Responsibilities of IRB Secretariat
Verify the Contents of the package
Review of protocol with vulnerable subjects as per the checklist provided
Fill assessment forms and submit one day prior to the meeting
Responsibilities of IRB members
IRB Meeting – record the IRB discussion and decision
IRB decision is communicated to the PI
Storage of original documents with relevant correspondence