



Institutional Review Board

University of Missouri-Columbia

Standard Operating Procedure

Recruitment of Special Subject Populations

## Recruitment of Special Subject Populations

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### Policy/Procedure

Federal Regulations require the selection of subjects to be equitable. In ensuring this requirement the IRB takes into account the purpose and the setting in which the research will be conducted. The board is cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. The regulations provide additional requirements to protect the welfare of children, prisoners, pregnant women, fetuses and neonates.

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The informed consents and assents for all vulnerable populations must still meet the requirements 45 CFR 46.116 and 21 CFR Part 50 Subpart B and Subpart D (please see the Policies on Informed Consent- Types and Elements and Process and Issues).

**Research involving Pregnant Women (45 CFR 46 subpart B)**

**45 CFR 46.204** - Pregnant women or fetuses may be involved in research if the IRB determines all of the following criteria are met:

- a) When scientifically appropriate, preclinical and clinical studies, have been conducted and provide data for assessing potential risks to pregnant women and fetuses
- b) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for:
  - The pregnant woman or the fetus
  - The risk to the fetus is not greater than minimal and the purpose of the research is to develop important biomedical knowledge that cannot be obtained by any other means
- c) Any risk is the least possible for achieving the objectives of the research
- d) If the research holds out the prospect of direct benefit to:
  - The pregnant woman
  - Both to the pregnant woman and the fetus,
  - No prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal
  - and the purpose is the development of important biomedical knowledge that cannot be obtained by any other means, the woman's consent must be obtain in accordance with the requirements for informed consent
- e) If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained;  
Except when the father's is:
  - unable to consent because of unavailability
  - incompetent
  - temporary incapacity
  - The pregnancy resulted from rape or incest
- f) Each person providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate
- g) For children who are pregnant, assent and permission are obtained in accord with [subpart D](#) (additional protections for children – see below)
- h) No inducements, monetary or otherwise, can be offered to terminate a pregnancy

- i) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy
- j) Individuals engaged in the research will have no part in determining the viability of a neonate.

**Research involving neonates**

Neonates of uncertain viability and nonviable neonates may be involved in research if the IRB determines all of the following criteria are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
2. Each person providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate
3. Individuals engaged in the research will have no part in determining the viability of a neonate.

**Research involving Neonates of uncertain viability:**

Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research unless the following additional conditions have been met:

- a) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, *or*
- b) The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research

The legally effective informed consent of both parents of the nonviable neonate must be obtained; a legally authorized representative of either or both of the parents is unacceptable. A waiver and/or alterations of the consent 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 neonate will suffice to meet the requirements, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest.

**Research involving Non-viable neonates:**

After delivery, nonviable neonate may not be involved in research unless all of the following additional conditions are met:

- a) Vital functions of the neonate will not be artificially maintained;
- b) The research will not terminate the heartbeat or respiration of the neonate;
- c) There will be no added risk to the neonate resulting from the research;
- d) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means

The legally effective informed consent of both parents of the nonviable neonate must be obtained; a legally authorized representative of either or both of the parents is unacceptable. A waiver and/or alterations of the consent 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 neonate will suffice to meet the requirements, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest.

**Research involving, after delivery, the placenta, the dead fetus or fetal material:**

Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.

If information associated with material is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent policies are applicable.

**Research not otherwise approvable for pregnant women and fetuses, or neonates:**

The research must present an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates.

IRB will approve the research only if:

- (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, fetuses or neonates; and
- (b) The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the FEDERAL REGISTER, has determined either:
  - (1) That the research in fact satisfies the conditions of §46.204, 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, fetuses or neonates;
    - ii. The research will be conducted in accord with sound ethical principles; and
    - iii. Informed consent will be obtained in accord with the informed consent policies.

**Children in Research:**

To approve the research, the research must meet one of the following categories:

**45 CFR 46.404 and 21 CFR 50.51**

- 1) The research is minimal risk
- 2) Adequate provisions are made to solicit the assent of the children and permission of the parents or guardians in accordance of 21 CFR 50.55 and or 45 CFR 46.408 (the IRB may find that the permission of one parent is sufficient\*)

**45 CFR 46.405 and 21 CFR 50.52**

- 1) The research is greater minimal risk, but presenting the prospect of direct benefit to an individual subject or by a monitoring procedure that is likely to contribute to the subject's well-being
  - i. the risk is justified by the anticipated benefit to the subject; and
  - ii. the relationship of risk to benefit is at least as favorable as any available alternative approach
- 3) Adequate provisions are made to solicit the assent of the children and permission of the parents or guardians in accordance of 21 CFR 50.55 and or 45 CFR 46.408 (the IRB may find that the permission of one parent is sufficient\*)

**45 CFR 46.406 and 21 CFR 50.53**

- 1) The research is greater minimal risk with no prospect of direct benefit, but likely to yield generalizable knowledge about the disorder or condition
  - i. the risk represents a minor increase over minimal risk
  - ii. the experience is reasonably commensurate with those in their actual or expected medical, dental, psychological, social, or educational situations
  - iii. the intervention is likely to yield generalizable knowledge about the disorder or condition that is of vital importance
- 4) Adequate provisions are made to solicit the assent of the children and permission of the parents or guardians in accordance of 21 CFR 50.55 and or 45 CFR 46.408 (two parent consent is required\*)

**45 CFR 46.407 (DHHS)**

Research that is not otherwise approvable, but which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children:

Research that is not approvable under one of the previous categories may be conducted or funded by DHHS provided that the IRB and the Secretary, after consultation with a panel of experts, finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a significant problem affecting the health and welfare of children. The panel of experts must also find that the research will be conducted in accordance with sound ethical principles and adequate provisions are made for soliciting the assent of children and the permission of the parents or guardians\*.

**21 CFR 50.54 (FDA related research)**

If the proposed research is regulated by the FDA and does not meet one of the previous categories the research may proceed only if:

- (a) The IRB finds and documents that the clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and

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(b) The Commissioner of Food and Drugs, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, determines either:

(1) That the clinical investigation in fact satisfies the conditions of 50.51, 50.52, or 50.53, as applicable, or

(2) That the following conditions are met:

(i) The clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;

(ii) The clinical investigation will be conducted in accordance with sound ethical principles; and

(iii) Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in 50.55\*.

**\*Consent and Assent Procedures** – see Informed Consent – Process and Issues SOP

### **Use of Prisoners in Research**

The IRB recognizes that research involving prisoners raises the issue of whether the subject's situation prohibits the exercise of free choice to participate in research and whether or not the prisoner's confidentiality will be adequately maintained. When reviewing research with the use of prisoners, minimal risk is defined as the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

The IRB shall determine the following:

- a) Have IRB staff assure that the person designated as the prisoner representative, (see IRB membership SOP), reviews all materials pertaining to the research and documents the information utilizing the reviewer checklist.
- b) The research MUST fit into one of the four categories:
  - i. Category I: Studies of the possible cause, effects, and processes of incarceration and criminal behavior, and involves no more than minimal risk with no more than inconvenience to the subjects;
  - ii. Category II: Studies of prisons as institutional structures or of prisoners as incarcerated persons, and involves no more than minimal risk no more than inconvenience to the subjects; ;
  - iii. Category III: Studies on particular conditions affecting prisoners as a class; (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological

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problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of his intent to approve such research; or

- iv. Category IV: Studies involving a therapy likely to benefit the prisoner subject: Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of the intent to approve such research.
- c) Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;
- d) The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
- e) Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project
- f) The information is presented in language which is understandable to the subject population
- g) Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and
- h) Where the Board finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.
- (i.) The Board shall carry out such other duties as may be assigned by the Secretary.
- (ii.) The institution shall certify to the Secretary, in such form and manner as the Secretary may require, that the duties of the Board under this section have been fulfilled.

For epidemiologic studies, the following must be true:

- The sole purposes are one of the following:
  - To describe the prevalence or incidence of a disease by identifying all cases.
  - To study potential risk factor associations for a disease
- The research presents no more than minimal risk and no more than inconvenience to the prisoner-subjects, and

- Prisoners are not a particular focus of the research.

**Modifications and Continuing Review:**

1. Minor modifications to research may be reviewed using the expedited procedure described below, using either of the two procedures described based on the type of modification.
2. Modifications involving more than a minor change reviewed by the convened IRB – must use the same procedures for initial review including the responsibility of the prisoner representative to review the modification and participate in the meeting (as described above).
3. Continuing review – must use the same procedures for initial review including the responsibility of the prisoner representative to review the continuing review materials and participate in the meeting (as described above).
  - a. If no participants have been enrolled, the research may receive continuing review using the expedited procedure under expedited category #8.

**Research using the Expedited Procedure, the IRB may use the following two options:**

1. For research involving interaction with prisoners reviewed by the expedited procedure:
  - a. Research involving interaction with prisoners may be reviewed by the expedited procedure, if a determination is made that the research involves no greater than minimal risk for the prison population being studied.
  - b. The prisoner representative must concur with the determination that the research involves no greater than minimal risk.
  - c. The prisoner representative must review the research as a reviewer, designated by the chair, or consultant. This may be as the sole reviewer or in addition to another reviewer, as appropriate.
  - d. Review of modifications and continuing review must use the same procedures for initial review using this expedited procedure including the responsibility of the prisoner representative.
2. For research that does not involve interaction with prisoners (e.g. existing data, record review) reviewed by the expedited procedure:
  - a. Research that does not involve interaction with prisoners may be reviewed by the expedited procedure, if a determination is made that the research involves no greater than minimal risk for the prison population being studied.
  - b. Review by a prisoner representative is not required.
  - c. The prisoner representative may review the research as a reviewer or consultant if designated by the IRB chair.
  - d. Review of modifications and continuing review must use the same procedures as initial review.

**If a participant becomes a prisoner while enrolled in a research study that was not reviewed according to Subpart C:**



1. Confirm that the participant meets the definition of a prisoner.
2. Terminate enrollment or review the research study under Subpart C if it feasible for the participant to remain in the study.
3. Before terminating the enrollment of the incarcerated participant, the IRB should consider the risks associated with terminating participation in the study.
4. If the participant cannot be terminated for health or safety reasons:
  - a. Keep the participant enrolled in the study and review the research under Subpart C.
    - i. If some the requirements of Subpart C cannot be met, but it is in the best interest of the participant to remain in the study, keep the participant enrolled and inform OHRP of the decision along with the justification.
  - b. Remove the participant from the study and keep the participant on the study intervention under an alternate mechanism such as compassionate use, off label use, etc.

### **Potential Subjects who may need additional Considerations**

#### **Mentally Disabled**

Cognitively impaired subjects can be temporarily impaired, from medication, a medical condition or other circumstance, or permanently impaired. The IRB appreciates the ethical concerns in research involving individuals that are cognitively impaired which may compromise their capacity to understand the information presented and their ability to make a reasoned decision about participating in research. When reviewing the study, the board will:

- a. determine if the subject population is appropriate for the study
- b. require the investigator to specifically describe the psychological or medical screening criteria
- c. Assure that the investigator satisfies the Informed Consent criteria:
  - a. Presume the subject is competent to consent unless there is evidence of serious mental disability that would impair reasoning or judgment.
    - i. Obtain consent from the legally authorized individual (see Informed Consent –Process and Issues SOP regarding Legally Authorized Representatives)
- d. seek the subject's assent where applicable
- e. assess the proposed plan for the determination of whether the participant has the capability to consent or assent and determine if the plan for assent is adequate
- f. if the subjects are institutionalized, the study must be reviewed full board
- g. determine if any additional safeguards are necessary
- h. seek a legal consultant to determine the applicable laws of the state, if needed

#### **Students and Employees**

The IRB recognizes the special concerns that may present when students and employees participate in research projects. The IRB will pay special attention to protect against coercion and offense to the voluntary requirement for research involving humans

For projects involving students that offer credit for participation:

- The investigator must provide a comparable (time and commitment) alternate method of credit for a student
- The student shall not lose the extra credit if they withdraw from the study
- Students must be assured that they will not be penalized and their grade will not be adversely affected by their decision to participate in the research.

Elderly and Economically or Educationally Disadvantaged Subjects

The IRB will assure that:

- a. Avoidance of coercion and undue influence upon subjects to participate;
- b. Assess the mechanism for offering incentives of value to the subjects:

International Research - see Policy on Transnational Research

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