Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
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Section: Vulnerable Populations
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Subject: Procedure for Special Categories of Research: Prisoners

Procedure:
This procedure outlines the responsibilities as mandated by the federal regulations when prisoners are involved as participants in research.

I. Investigator Responsibilities.
   A. The Investigator will submit supplemental information with any new study submission in which prisoners will be a target population for research activities. If the participant population has an increased potential to become prisoners, and the Investigator will be interacting, intervening, or collecting identifiable private information during the incarceration, the Investigator may choose to have the proposal reviewed initially by the IRB and OHRP for prisoner participation.
   B. The Investigator must report in writing to the IRB immediately when a participant becomes a prisoner after enrollment in research activities. If the research was not reviewed and approved by the IRB and OHRP in accordance with 45 CFR 46 Subpart C, the Investigator must notify the IRB in writing of the event. All research interactions and interventions with, and obtaining identifiable private information about, the now incarcerated prisoner-participant must cease until the requirements of Subpart C have been satisfied with respect to the relevant research activities.
   NOTE: The IRB Chairperson may determine that the subject may continue to participate in the research until the requirements of Subpart C are satisfied in special circumstances in which the Investigator asserts that it is in the best interests of the subject to remain in the research study while incarcerated.
   C. Investigators are responsible for obtaining and providing documentation of approval from the detention or correctional facility involved (i.e., prisons, jails, workhouses, etc.) to the IRB.
   D. The Investigator will provide any additional documents or materials required for certification to the Secretary (through OHRP) for Federally funded research involving prisoners.
   E. The Investigator may not screen, recruit, or enroll any individual involuntarily confined or detained in a penal institution without written IRB approval. If the biomedical or behavioral research is conducted or supported by HHS, it also requires review and written approval by the Secretary (through OHRP) before any research activities may begin, including screening and enrollment.

II. IRB Committee Responsibilities.
   A. The IRB Committee must review the proposed research taking into consideration all applicable policies and procedures, as well as the additional requirements for prisoners to participate in research as described in 45 CFR 46, Subpart C.
   B. The Committee may not review or make determinations regarding studies involving prisoners as a target population unless the Committee has a member who is a prisoner or a prisoner representative with a close working knowledge, understanding and appreciation of prison conditions from the perspective of the prisoner. Documentation of expertise is provided by the curriculum vitae of the prisoner or prisoner representative serving on the IRB.
   C. The IRB Committee will review the proposed research, consents, and applicable
documents to determine whether the study meets criteria 45 CFR 46.111 and 21 CFR 56.111 for approval. In order to provide written documentation of these criteria, the Primary Reviewer must complete the “Reviewer’s Comments” detailing how each of these criteria is met. In addition, the IRB will discuss the additional protections necessary for this population as outlined in the supplemental information provided by the Investigator. The Primary Reviewer will be responsible for documenting these additional protections on the “Supplemental Reviewer’s Comments for Prisoners” form. All seven criteria for approval must be met and documented individually.

D. When a research participant becomes a prisoner, and the IRB has not previously reviewed the proposal for prisoner populations, the IRB will conduct a review of the research proposal in accordance with Subpart C and make one of the following determinations:

1. IRB review and approval is not required if the research interactions and interventions or obtaining of identifiable private information will not occur during the incarceration period or
2. Approve withdrawal of the participant(s) from the study if withdrawal will not place the participant at undue harm or risk; or
3. Approve research participation for non-prisoner participants but approve pending for prisoner-participants if the seven required findings in 45 CFR 46.305(a) have been met but the IRB is still waiting on the receipt of the Secretary’s determination (through OHRP) that the proposed research falls within the categories of research permissible under 45 CFR 46.306(a)(2). All interactions and interventions with, and obtaining identifiable private information must cease for these prisoner-participants until the requirements of Subpart C have been satisfied with respect to the relevant protocol. **NOTE:** OHRP has allowed one important exception. In special circumstances in which the Principal Investigator asserts that it is in the best interests of the participant to remain in the research study while incarcerated, the IRB Chairperson may determine that the subject may continue to participate in the research until the requirements of Subpart C are satisfied.

4. Approve research participation for non-prisoner participants but defer for prisoner-participants if the seven required findings in 45 CFR 46.305(a) have not been met to the satisfaction of the IRB. All interactions and interventions with, and obtaining identifiable private information must cease for these prisoner-participants until the requirement of Subpart C have been satisfied with respect to the relevant protocol. **NOTE:** OHRP has allowed one important exception. In special circumstances in which the Principal Investigator asserts that it is in the best interests of the participant to remain in the research study while incarcerated, the IRB Chair may determine that the subject may continue to participate in the research until the requirements of subpart C are satisfied.

E. For DHHS supported research, the institution must certify to the Secretary (through OHRP) that the IRB designated under its assurance of compliance has made the seven findings required under 45 CFR 46.305(a) and a statement indicating that the IRB chose one of the four permissible categories of research in 45 CFR 46.306(a)(2) or the epidemiological waiver.

1. It is sufficient to include a statement that indicates that the IRB made the required findings under 45 CFR 46.305(a). OHRP does not require that the prisoner letter include a specific listing or rationale behind the IRB findings. The institution may wish to include a brief, protocol-specific explanation of the IRB’s rationale for each finding.

2. The institution must indicate in the certification letter which of the four categories of permissible research involving prisoners in 45 CFR 46.306(a)(2) is applicable to the proposed research. Research involving prisoners can proceed only if the research fits under a category of
permitted research under 45 CFR 46.306(a)(2). See attached “Category-Specific Information for Permissible Research” for additional requirements. OHRP will make its own determination, based on the information in the prisoner certification letter, the protocol materials and the grant application as to whether any of the four categories apply to the proposed research. OHRP may or may not concur with the IRB’s choice of category.

3. The institution may wish to include a statement that indicates that the IRB was constituted as per the requirements in 45 CFR 46.304. OHRP does not require that the prisoner certification letter include information about the manner in which the IRB fulfills the requirements of 45 CFR 46.304. The institution may wish to provide the name of the prisoner representative.

4. In addition to the prisoner certification letter, the following information must also be sent to OHRP:
   a) The protocol application (which includes the protocol and any IRB submission materials including the ICDs); and
   b) The grant application (including any grant award updates).

5. OHRP encourages the inclusion of the following information with the prisoner certification letter:
   a) OHRP Assurance # and IRB #;
   b) Site(s) where research involving prisoners will be conducted;
   c) If prisoner research site is “engaged in research”, provide OHRP Assurance #;
   d) DHHS Grant Award # and Agency Name;
   e) Funding Agency Grants/Program Officer Name and Telephone #;
   f) Title of DHHS Grant and protocol, if different;
   g) Version date of the ICD to be used with prisoners;
   h) Date(s) of IRB Meeting(s) in which the protocol was considered and provide a chronology of:
      (1) Date of initial IRB review; and/or
      (2) Date of Subpart C reviews including:
          (a) Type of IRB review (initial, amendment, addendum,
              continuing review); and
          (b) Special IRB review for prisoner issues.
   i) Principal Investigator; and
   j) Reason for IRB review (choose the applicable reasons):
      (1) Non-prison study (not previously reviewed and certified under Subpart C) in which participant has become incarcerated (or otherwise fits the definition of prisoner in 45 CFR 46.303(c)) and the PI wishes to continue the individual’s participation in the study.
      (2) Non-prison study with at-risk population (i.e., probationers, substance abusers);
      (3) Non-prison study, majority of study population are non-prisoners but PI seeks to enroll some prisoners (as defined in 45 CFR 46.303(c));
      (4) Minimal risk DHHS conducted or supported epidemiologic research, majority of study population are non-prisoners but PI seeks to enroll some prisoners (prisoners are not the focus of the study) and the sole purpose of the study is either:
          (a) To describe the prevalence or incidence of a disease by identifying all cases or
          (b) To study potential risk factor associations for a disease.
      (5) Initial Subpart C review of study designed to be conducted in a prison or using prisoners as defined in 45 CFR 46.303(c), the PI seeks to enroll already incarcerated subjects.

6. It would be helpful (but not required) if the prisoner certification letter contained the following information:
   a) Justification for the use of prisoners in the study. If applicable, delineate the protocol to be conducted in the prison from the overall project described in the grant application.
   b) Study objectives or study aims and a brief summary;
c) Customary treatment or services at the prison (or alternative to incarceration) research site(s) for the condition being studied;
d) Description of how risks specific to a prison (or alternative to incarceration) setting are minimized;
e) Whether the prison site(s) are “engaged in research” and whether they have obtained an assurance with OHRP;
f) Whether a Certificate of Confidentiality was obtained by the PI for the study.
g) Describe recruitment procedures in the specific prison (or alternative to incarceration) setting; and/or
h) Describe how the consent form was altered for use with a prison population or specific prisoner and whether the subsequently incarcerated participant will be re-consented

7. All prisoner research certification letters should be mailed to:
OHRP Prisoner Research Coordinator
Office for Human Research Protections (OHRP)
Department of Health and Human Services
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

F. The IRB Committee may approve the research for non-prisoner populations until all the criteria in Subpart C are satisfied.

G. The IRB must inform the Investigator in writing that no prisoner-subjects can be enrolled or involved until the IRB/institution receives a letter from OHRP that acknowledges receipt of the prisoner certification and indicates the Secretary’s (through OHRP) determination that the proposed research falls within the categories of research permissible under 45 CFR 46.306(a)(2).

III. Regulatory Compliance Analyst (RCA) Responsibilities.
A. The RCA will verify that supplemental information is completed by the Investigator as part of the initial study documents.
B. The RCA will conduct a pre-review and take into consideration the requirements under 45 CFR 46, Subpart C, under which prisoners may participate in human subjects research.
C. The RCA will notify the Investigator with any questions or needed clarification in regards to the prisoner population.
D. The RCA will verify that the Committee reviewing the research involving a prisoner has at least one member who is a prisoner or prisoner representative in attendance.
E. To adequately document the IRB review of the research:
1. The curriculum vitae of the prisoner or prisoner representative serving on the IRB will be on file in the IRB
2. The “Supplemental Reviewer’s Comments for Prisoners” will be placed in the IRB file and
3. The discussion and determinations of the IRB regarding the seven additional findings required under HHS regulations at 45 CFR 46.305(a) will be documented in the minutes.
F. The RCA will assist in preparing documents for the certification letter and prepare a draft certification letter to the Secretary (through OHRP) which will be signed by the appropriate institutional official listed on VU or VUMC’s FWA
If the IRB choses category (i) or (ii), (after determining that the study satisfied the threshold condition for the category), OHRP recommends that the IRB provide the rationale for determining that the study is no more than the Subpart C definition of minimal risk. It would also be helpful if the letter provided the IRB reasoning for the choice of this category.

If the IRB choses category (iii), thus triggering the requirement for Secretarial consultation with appropriate experts, OHRP recommends that the IRB provide the rationale for the choice of category and formally request that consultation in the letter.

If the IRB choses category (iv), OHRP recommends that the IRB provide the rationale for determining that the study is "research on practices...which have the intent and reasonable probability of improving the health and well being of the subject."

- OHRP recommends that the “practice” be described; typically, it will be an intervention being studied.
- If the study is an extension study or is a free-standing follow-up study to another study that involves an intervention, OHRP recommends that the IRB describe the relationship between this study and the study with the intervention.

Regarding category (iv), describe whether the study involves assigning prisoners to control groups which may not benefit.

- If all subjects will be recruited and assigned to study groups (including a control group) prior to incarceration, then "prisoners" will not assigned to a control group. Therefore, if the IRB is being asked to review a study under Subpart C because a previously enrolled subject now meets the Subpart C definition of “prisoner” and IR wishes to continue the participation of this prisoner-subject, there will be no trigger for a Secretarial consult if the IRB finds that the study fits under category iv.
- If the study DOES involve assigning persons that meet the Subpart C definition of “prisoner” to a control group “which may not benefit from the research”, the requirement for Secretarial consultation with appropriate experts is triggered.

Explanation of category (iv) phrase “control groups which may not benefit from the research”:

- If there is a study arm that provides treatment-as-usual, services-as-usual or the standard medical care that would available to the prisoner whether or not he/she participated in the study, this type of study arm would be considered a “control group” under Subpart C, category iv (45 CFR 46.306(a)(2)(iv)).

- The presence of a control group to which persons meeting the Subpart C definition of “prisoner” may be assigned triggers a Secretarial consultation with experts, which must occur after OHRP receives the prisoner certification and prior to the involvement of any “prisoners” in the study.

- If there is a study arm that provides an intervention in addition to treatment-as-usual, or services-as-usual or standard medical care, OHRP would probably not consider this type of study arm a Subpart C category iv “control group”.

Information about the June 20, 2003 Waiver of the Applicability of Certain Provisions of DHHS Regulations for the Protection of Human Subjects for DHHS Epidemiologic Research Involving Prisoners as Subjects

- For a minimal risk epidemiologic study in which prisoners are not the particular focus and the sole purpose of the study is either:
  - To describe the prevalence or incidence of a disease by identifying all cases or
  - To study potential risk factor associations for that disease.

- The two Subpart C provisions that are waived are:
  - The requirement that an IRB choose one of the four categories in 45 CFR 46.306(a)(2); and
An institution/IRB must certify in writing to OHRP, even if the June 20, 2003 Subpart C epidemiological waiver applies.

- The prisoner certification letter for an epidemiological study that falls under the waiver must contain the following statements:
  - The IRB fulfilled its duties under 45 CFR 46.305(a)(2)-(7);
  - The research is no more than minimal risk or inconvenience; and
  - Prisoners are not the particular focus of the study.

- It would be helpful if the letter also contained a statement as to the sole purpose of the study, as contained in the protocol and/or grant application materials.