Wayne State University Human Investigation Committee	
Subject	Vulnerable Participants: Prisoners
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Background

Prisoners may be under constraints because of their incarceration, which could affect their ability to make a truly voluntary and un-coerced decision whether or not to participate in research. Therefore, federal regulation 45 CFR 46 provides additional protection for prisoners involved in research. These are outlined in the 45 CFR 46, Subpart C – Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Participants. While these regulations pertain only to research supported by the Department of Health and Human Services (DHHS), the Wayne State University (WFU) Federal Wide Assurance extends the same protection to all research participants regardless of financial support or funding.

In lay terms, prisoners are people who are involuntarily being held in a jail, prison, treatment or other facility as described herein or who have been detained while awaiting arraignment, trial, or sentencing. This includes those who have been admitted to hospitals, psychiatric centers, alcohol or drug treatment facilities, or confined to their home under a court order. The definition applies to children as well as adults. When children are involved, the additional protections outlined in both Subpart C and Subpart D (Children) apply and must be followed.

Scope

This policy/procedure applies to all investigators conducting research with prisoners regardless of age. For research projects that involve more than minimal risk, the Institutional Review Board (IRB) may consider whether there is the potential for direct benefit for the individual participant. More than minimal risk research projects in which there is only potential benefit to society or where the prison population is chosen as a convenient study population are not sufficient justifications for the enrollment of prisoners in a research project. Prisoners may not be enrolled in a research project involving a placebo unless the standard of care for the disease or condition is “no treatment” and the procedures for using the placebo are the same as the “no treatment” option.

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, may not be 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. Involvement in a research protocol cannot be considered as part of a parole hearing for any prisoner who has voluntarily agreed to be a research participant.

The primary issue surrounding the participation of prisoners in research has always been whether prisoners have a voluntary choice regarding their participation in research, or whether their situation prohibits the exercise of free choice. A secondary issue is whether confidentiality of participation and of data can be adequately maintained in the prison facility. Because the research participant is not able to prioritize his/her schedule, the principal investigator is required to obtain additional concurrence and when necessary to make alternate arrangements so that the research participant would be able to meet with the investigative team.

Research involving prisoners may not be conducted by Veterans Administration (VA) investigators while on official duty, or at VA-approved off-site facilities unless a waiver has been granted by the Chief Research and Development Officer. If the waiver has been granted the research must follow all federal, state, and local regulations and WSU policy (1200.05 47).

Definitions

Administrative Approval – Review and approval by the WSU Office of the Vice President for Research (OVPR).

DHHS – The Department of Health and Human Services [46.303(b)].

Minimal Risk – 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 of healthy persons [46.303(d)].

OHRP – Office of Human Research Protection.

Prisoner – Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statue; as well as individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing [46.303(c)].

Prisoner Subcommittee – A subcommittee of the Human Investigation Committee (HIC) appointed by the Associate Vice President for Research to review all protocols in which principal investigators propose to enroll prisoners. At least one member of the prisoner subcommittee shall have background and experience with prisoners or the penal systems.

Secretary – The Secretary of Department of Health and Human Services (DHHS) and any other officer or DHHS employee to whom authority has been delegated [46.303(a)].

HIC Policy/Procedures

Federal Regulations

[45 CFR 46.306] Permitted research involving prisoners include:

1. Biomedical or behavioral research conducted or supported by DHHS may involve prisoners as subjects only if:
    a. The institution responsible for the conduct of the research has certified to the Secretary that the Institutional Review Board has approved the research under 45 CFR 46.305 of this subpart; and
    b. In the judgment of the Secretary the proposed research involves solely the following:
        i. The research is the study of possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
        ii. The research involves the study of prisoners as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
        iii. The research involves the study of conditions particularly 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 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;
        iv. 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.
        v. Secretarial Waiver – The DHHS Secretarial waiver for certain epidemiological research conducted or supported by DHHS functions as a fifth category of permissible research (68 FR 36929, June 20, 2003). The criteria for this category are that the research must have as its sole purpose
            - to describe the prevalence or incidence of a disease by identifying all cases, or
            - 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.
            - prisoners are not a particular focus of the research.

The institution still must review the research under subpart C and certify to OHRP that an appropriately constituted IRB has reviewed the proposal and made all other required findings under HHS regulations at 45 CFR 46.305(a) and receive OHRP authorization prior to initiating any research involving prisoners. All of the other requirements of subpart C apply to research in this category.

vi. Except as provided in paragraph (1.) of this section, biomedical or behavioral research conducted or supported by DHHS shall not involve prisoners as subjects.

Reporting Requirements for DHHS Supported Research

For all research involving prisoners that is supported or conducted by DHHS, regardless of category, WSU must certify to the Secretary through OHRP that the IRB reviewed the research and made seven findings as required by the regulations (45 CFR 46.305(a)(1) (see below "***What the IRB Must Determine in Order to Approve Prisoner Research***"). After the certification request is sent to OHRP, OHRP must then determine whether the proposed research involves one of the categories of research permissible under 45 CFR 46.306(a)(2), and if so, which one. Following certification, OHRP will send a letter to the institution authorizing the involvement of prisoners in the proposed research, if OHRP finds that the research involves one of the permissible categories.

- Each institution engaged in a multi-center research study must certify to the OHRP that DHHS regulations at 45 CFR 46.305© and 46.306(a)(1) have been met unless an institution relied on the review of an IRB operated by another institution engaged in the research, and that IRB or the other institution certified to OHRP on behalf of both institutions.
- If research is not conducted or supported by DHHS, WSU does not need to submit any certification to OHRP
- Research proposals that are supported or conducted by DHHS and are in category iii, iv, or v, require a Secretarial consultation, in addition to certification to OHRP. OHRP, on behalf of the Secretary of DHHS, will consult with appropriate experts with respect to the applicable category. When applicable, OHRP will also publish a notice of intent to approve such research in the FEDERAL REGISTER. Research can proceed only after receiving an authorization letter from OHRP.
- When approval from OHRP and/or the Secretary of DHHS is required before prisoners can be enrolled in research, the WSU OVPR will be responsible for submitting the protocol and related documents for certification and consultation.

Conditions for Enrollment of Prisoners:

- Prisoners may not be enrolled in a research project involving a placebo unless the standard of care for the disease or condition is "no treatment" and the procedures for using the placebo are the same as the "no treatment" option.
- Secretarial waiver of informed consent in certain emergency research is not applicable to research involving prisoners (61 FR 51531).
- None of the exemption categories in the DHHS regulations for research [45 CFR 46.101(b)] apply to research involving prisoners [45 CFR 46.101(i), Footnote 1]. Research that requires expedited or full board review for non-prisoners may enroll prisoners in a research protocol if reviewed and approved by all of the following: (1) one of the IRB Committees; (2) the WSU Prisoner

Subcommittee; Research that qualifies for exemption from IRB review may not enroll prisoners. Research that requires expedited or full board review for non-prisoners may enroll prisoners in a research protocol if reviewed and approved by **all** the following: (1) one of the WSU IRBs at a full board meeting; (2) the WSU HIC Prisoner Subcommittee; and (3) after administrative review by the Institutional Official.

- If a Principal Investigator (PI) has requested approval to enroll prisoners in a research project in addition to other research participants, the enrollment of other research participants may be started after IRB review and approval. The enrollment of prisoners may not begin until after the additional approval of: (1) the Prisoner Subcommittee and (2) the Institutional Official.
- This process applies also if a PI enrolls a participant in a research protocol who subsequently becomes a prisoner. When this occurs, the individual's participation in the research must stop unless the PI determines that withdrawing the participant will cause harm to the participant. In any case, the PI must notify the HIC immediately for instructions on how to proceed in obtaining IRB and administrative approval for enrolling prisoners in a research protocol.
- Because the prison or penal institution or other facility responsible for the care of the prisoner must participate in the implementation of the research protocol, the PI is responsible for obtaining the initial approval of the prison or penal institution. The letter of support must contain:
    - A general statement of support for the PI to conduct the research in their institution;
    - An assurance that the prisoner will not be given any advantages from participation when compared to the other prisoners who do not participate;
    - An assurance that participation in the research will not influence the parole board and its decisions; and
    - A statement that the protocol meets the local standards for the ethical treatment of prisoners.
- Once initial approval of the prison or penal institution administrative unit has been obtained and the protocol has been approved by the IRB for the enrollment of prisoners in the research project, the WSU OVPR shall determine if the letter of support form that institution is sufficient.
- A separate informed consent form that takes into account the additional risk and uniqueness of being a vulnerable population shall be developed by the PI for the enrollment of prisoners, approved by one of the WSU IRBs at a full board meeting, and the Prisoner Subcommittee. That informed consent form must be used for all prisoners but cannot be used for individuals who are not prisoners.
- For Department of Defense (DoD) regulated research involving prisoners:
    - The DoD prohibits research involving prisoners of war.
    - The IRB must be aware of the definition of "prisoner of war" for the DoD component granting the addendum.

Composition of Institutional Review Boards When Prisoners are Involved:

- A majority of the Board (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the Board.
- At least one member of the Board shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that when more than one Board reviews a particular research project, only one Board need satisfy this requirement.

Review of "Greater Than Minimal Risk" Research Involving Prisoners:

For research reviewed by the convened IRB (research that is greater than minimal risk), involving prisoners:

- The prisoner representative must be a voting member of the IRB.
- The prisoner representative must review research involving prisoners (i.e., the prisoner representative must receive all materials pertaining to the research—same as primary reviewers).
- The prisoner representative must be present at a convened meeting when the research involving prisoners is reviewed. If the prisoner representative is not present, research involving prisoners cannot be reviewed or approved.
- The prisoner representative must present his/her review either orally or in writing at the convened meeting of the IRB when the research involving prisoners is reviewed.
- Minor modifications may be reviewed using the expedited procedure described below, using either of the two procedures described based on the type of modification.
- Substantial modifications reviewed by the convened IRB must use the same procedures for initial review including the responsibility of the prisoner representative.
- Continuing review of research involving prisoners must use the same procedures for initial review, including the responsibility of the prisoner representative.

Review of "Minimal Risk" Research Involving Prisoners:

For research reviewed by the expedited procedure (minimal risk) involving interaction with prisoners (including obtaining consent from prisoners):

- Research involving prisoners, involving interaction with prisoners (including obtaining consent from prisoners) may be reviewed by the expedited procedure if a determination is made that the research is minimal risk for the prison population being studied or included.
    - The prisoner representative must concur with the determination of minimal risk.
- The prisoner representative must review the research as a reviewer or consultant. This may be as the sole reviewer or in addition to another reviewer or in place of another reviewer, as appropriate.
- Review of modification and continuing review must use the same procedures for initial review using this expedited process, including the responsibility of the prisoner representative.

Review of research that does not involve interaction with prisoners:

For research reviewed by the expedited procedure that does not involve interaction with prisoners (e.g., existing data, record review):

- Research involving prisoners that does not involve interaction with prisoners may be reviewed by the expedited procedure, if a determination is made that the research is minimal risk for the prison population being studied or included.
- The prisoner representative may review the research as a reviewer or consultant if designated by the IRB chair, but review by the prisoner representative is not required.
- Review of modification and continuing review must use the same procedures for initial review using this expedited process including the responsibility of the prisoner representative.

What the IRB Must Determine in Order to Approve Prisoner Research:

When an IRB is reviewing a protocol in which a prisoner is a subject, the IRB must make, in addition to other requirements under 45 CFR 46, Subpart A, seven additional findings under 45 CFR 46.305(a), as follows:

1. The research under review represents one of the categories of research permissible under 45 CFR 46.306(a)(2);
2. 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;
3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
4. 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 IRB 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;
5. The information is presented in language which is understandable to the subject population;
6. 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
7. Where the IRB 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.

When an enrolled participant becomes a prisoner

The regulatory protections are applicable to all prisoner participants, regardless of their status at the time of enrollment in a study. OHRP does not require immediate suspension of research activities when an enrolled participant becomes a prisoner. Rather, OHRP recommends for treatment and intervention studies that:

- Investigators inform the IRB immediately upon learning that a participant has entered prison and provide justification if the participant should remain in the research study;
- The IRB review the protocol "at the earliest opportunity" to determine whether continued participation in the research is appropriate under the regulations; and
- The IRB follow appropriate regulations to get approval or the study participant be removed from the study.

Typical Process for Enrolling Prisoners in a Research Protocol

1. The PI determines that he/she would like to enroll prisoners in a research protocol.
2. The PI obtains initial approval in writing form the prison or penal institution concerning the enrollment of one or more prisoners in a research project.

3. In preparing the documentation for IRB initial submission, the PI checks “Prisoner” in the Vulnerable Participant section of the Protocol Summary Form and completes Appendix E. If a previously approved protocol is changed to now request enrollment of prisoners as research participants, the PI must complete an Amendment Form, and Appendix E of the Protocol Summary Form, for IRB review.
4. The PI prepares a separate consent form for the enrollment of prisoners in a research protocol.
5. The Protocol Summary Form or Amendment Form, informed consent form(s), penal institution approval letter, protocol, and accompanying documentation are submitted to one of the WSU IRBs.
6. The IRB reviews the protocol; may request additional clarification and/or modifications; and subsequently provides approval or disapproval for the enrollment of research participants in the protocol. If approved, the IRB shall indicate that the protocol must obtain review and approval of: (a) the Prisoner Subcommittee; and (b) Administrative Approval.
7. The Prisoner Subcommittee of the HIC shall review the protocol, may request additional clarification and/or modifications, and subsequently provide approval or disapproval. Special attention shall be paid to the consent form that is proposed to be used for all prisoners and to whether prisoners can be enrolled in the research under the guidelines of 45 CFR 46 Subpart C. The Prisoner Subcommittee shall determine if the Secretary of DHHS shall be required to approve the protocol. If “approved” the protocol is reviewed by the WSU Office of the Vice President for Research for administrative approval.
8. As part of the administrative approval, the OVPR shall: (a) determine if the institution would like to proceed with the enrollment of prisoners in the research project; (b) determine whether the Secretary of DHHS shall be required to approve the protocol, and if so, secure that approval; and (3) enter into an agreement with the prison, penal institution, treatment or other facility concerning their responsibilities.
9. If the Secretary of DHHS is required to approve the protocol, the OVPR shall be responsible for coordinating and submitting the materials necessary for DHHS review.
10. After obtaining: (a) the approval of one of the WSU IRBs to enroll human participants in a research protocol; (b) the approval of the Prisoner Subcommittee for the enrollment of prisoners in a research protocol; and (c) Administrative Approval to enroll prisoners in a research protocol, the PI is authorized to enroll prisoners in a research protocol.