Research with Vulnerable Populations

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1. PURPOSE

1.1. There are a number of ***research*** populations described in the Federal regulations and guidance as vulnerable and that require additional considerations or protections. Federal regulations describe the following groups as vulnerable: pregnant women, human fetuses and neonates; children; prisoners; economically and/or educationally disadvantaged; and, mentally disabled persons. Federal guidance also describes special protections for cognitively impaired persons, students and employees, terminally ill subjects, and persons with AIDS/HIV. The purpose of this document is to describe the ***policy*** and ***procedure*** for Institutional Review Board (IRB) review of research involving vulnerable populations and to provide guidance for ***researchers*** who intend to include vulnerable subjects in their projects.

2. DEFINITIONS

2.1. ***Children (***or ***Minors):*** individuals who have not attained the legal age for consent within the jurisdiction in which the research will be conducted.

2.2. ***Experimentation:*** an activity that is designed to explore or develop new or unproven teaching methods or techniques and is a sub-set of ***human subject research*** where there is an ***interaction*** or ***intervention*** with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction.

2.3. ***Fetus:*** the product of conception from implantation until delivery.

2.4. ***Neonate:*** a newborn from birth to 30 days.

2.5. ***PHS agencies:*** agencies funded by the Public Health Service (PHS) which include the National Institutes of Health (NIH), Food and Drug Administration (FDA), Substance Abuse and Mental Health Services Administration (SAMHSA), Agency for Healthcare Research & Quality (AHRQ), Agency for Toxic Substances and Disease Registry (ATSDR), Centers for Disease Control and Prevention (CDC), Health Resources and Services Administration (HRSA), and Indian Health Service (IHS).

2.6. ***Pregnant woman:*** A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery. Pregnancy encompasses the period of time from implantation until delivery.

2.7. ***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 statute, 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.

2.8. ***Prisoner of War (DoD):*** any person captured, detained, held, or otherwise under the control

of DOD personnel (military, civilian, or contractor employee). Such persons include: Enemy Combatant, Lawful Enemy Combatant, Unlawful Enemy Combatant, Enemy Prisoner of War, Retained Person., and Civilian Internee. Such persons do not include personnel of the DOD being held for law enforcement purposes.

2.9. ***Vulnerable population:*** a population whose members may have limited ***autonomy*** and/or who are at risk for coercion or undue influence.

3. GENERAL POLICY

3.1. In order to review ***federally-supported*** or FDA-regulated research with vulnerable populations, the IRB must have at least one member knowledgeable about and experienced in working with these populations.

3.2. If the research involves interventions or interactions with persons having cognitive impairment, there must be anticipated direct benefit for the participant or the objectives of the research cannot be met by means of inclusion of subjects who are capable of providing consent.

3.3. When research on vulnerable subjects is conducted outside the state of Georgia, the researcher is responsible to identify the local law(s) applicable to the determination of ***legally authorized representative***.

3.4. Researchers should be aware of the numerous ethical concerns presented by including populations with AIDS/HIV, including considerations of ***confidentiality***, ***privacy*** and ***justice*** and must follow applicable State regulations.

3.4.1. Research supported by PHS agencies requires that individuals whose test results are associated with personal identifiers be informed of their HIV test results and provided the opportunity to receive counseling, unless the situation is a special circumstance calling for an exception (e.g. , compelling evidence that a given individual would attempt suicide if informed that he/she is seropositive).

3.5. When research that presents an opportunity to understand, prevent, or alleviate a serious problem affecting children, pregnant women, neonates, or fetuses is not otherwise approvable by the UGA IRB, but because the research is not subject to regulatory approval and no government agency will conduct a review of this research to determine whether it can be approved, the ***Institution*** will conduct its own review that closely parallels the regulatory review process. See *Policy and Procedures: Review of Not Otherwise Approvable Research*.

3.6. **POLICY FOR RESEARCH INVOLVING PRISONERS**

3.6.1. The IRB must meet these composition requirements for all types of review by the convened IRB, including initial review, continuing review, and review of modifications to approved research.

3.6.1.1. At least one voting member of the Board shall be a ***prisoner***, or a ***prisoner*** representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one Board, only one Board need to satisfy this requirement.

3.6.1.2. A majority of the IRB (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the IRB.

3.6.2. ***Minimal risk*** for prisoners is defined by the regulations 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.

3.6.3. Exempt determination does not apply to research involving prisoners. See footnote 1, http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.101(b)(2).

3.6.4. For federally supported research, the UGA IRB complies with the additional requirements of Subpart C to the extent the sponsoring agency has adopted these standards.

3.6.5. Research supported by the Department of Justice (DOJ) and conducted within the Federal Bureau of Prisons may not involve medical ***experimentation***, cosmetic research, or pharmaceutical testing. Additional criteria must also be met (see *WORKSHEET: Additional Federal Criteria*).

3.6.6. For research supported by the DoD, there are additional protections and restrictions for inclusion of prisoners. See *WORKSHEET: Additional Federal Criteria*.

3.6.6.1. If the research involves prisoners (but not prisoners of war), the convened IRB must review; review by ***Expedited procedure*** is not allowed.

3.6.6.2. Prisoners of war or detainees may not be included in research. This exclusion does not include persons being held primarily for law enforcement purposes, except where the United States is the occupying power. This prohibition does not apply to activities covered by investigational new drug or investigational device provisions for the purpose of diagnosis or treatment of a medical condition in a patient. Such treatment (e.g., an investigational new drug) may be offered to detainees with the detainees' informed consent when the medical products are subject to FDA regulations for investigational new drugs or investigational medical devices, and only when the same product would be offered to members of the U.S. Military Services in the same location for the same medical condition and only when consistent with established medical practice involving investigational drugs and devices.

3.6.7. For research not federally supported or FDA regulated, the UGA IRB has developed standards that are intended to provide protections equivalent to those described in federal regulations.

3.6.7.1. Research involving prisoners that does not involve intervention but are limited to interactions or use of data/specimens (e.g., existing record review, surveys, interviews) may be reviewed using the expedited procedure if:

3.6.7.1.1. a determination is made that the research poses no more than minimal risk to the prisoners being studied or included, and

3.6.7.1.2. the research meets the criteria for expedited review.

3.6.7.2. For a submission that may be reviewed using the expedited procedure, the prisoner representative will review the research as the ***subject matter expert***.

3.6.7.3. Review of minor ***modifications*** *to approved research* and ***continuing review*** via expedited procedures may involve review by the prisoner representative as a subject matter expert, but is not required.

3.6.7.4. Non-federally supported research involving prisoners do not require a UGA consultation with DHHS Secretary or the submission of any certification to OHRP.

3.7. **POLICY FOR RESEARCH INVOLVING PREGNANT WOMEN, FETUSES OR NEONATES**

3.7.1. For federally supported research, the UGA IRB complies with all of the requirements in Subpart B to the extent the sponsoring agency has adopted these standards.

3.7.2. For research supported by or intended for submission to the EPA (Environmental Protection Agency), the study must not involve the intentional exposure of pregnant women or nursing women to any substance and requires compliance with 40 CFR 26 Subpart C for inclusion of pregnant women in observational research.

3.7.3. For research supported by the DoD, there are additional protections and restrictions for inclusion of pregnant women and fetuses**.** See *WORKSHEET: Additional Federal Criteria*.

3.7.4. For research not federally supported or FDA regulated, the UGA IRB has developed standards that are intended to provide protections equivalent to those described in federal regulations.

3.7.4.1. Permissible research involving pregnant women, fetuses or neonates includes research intended to generate "generalizable" or "scientific" knowledge, rather than limiting permissible research to that intended to generate important biomedical knowledge."

3.8. **POLICY FOR RESEARCH INVOLVING CHILDREN**

3.8.1. Minimal risk for research with children means 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 by average, healthy, normal children, taking into account their ages, maturity, and psychological state.

3.8.2. Children may be involved in research in all exempt categories with the exception of

DHHS Category 2. See *Policy and Procedures: Exempt Research*.

3.8.2.1. Regarding DHHS Category 2: Exempt determination does not apply to federally-sponsored research with children involving survey, interview, or observation of public behavior (when the investigator is participating in the activities being observed). See footnote 1, http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.101(b)(2).

3.8.3. For federally supported non-exempt research involving children, UGA IRB applies 46 CFR Subpart D to studies to the extent the sponsoring agency has adopted these standards.

3.8.4. For research not federally supported or FDA regulated, the UGA IRB has developed standards that are intended to provide protections equivalent to those described in federal regulations.

3.8.5. For non-federally supported non-exempt research involving children, the IRB may waive the requirements in Subpart D such as obtaining parental permission where:

3.8.5.1. the procedures do not ordinarily require parental permission outside of the research context;

3.8.5.2. the investigator has presented evidence that prospective participants have the capacity to provide informed consent when taking into account their ages, maturity, and psychological state (e.g., a student who is attending a postsecondary institution); and,

3.8.5.3. appropriate safeguards are in place.

3.8.6. FDA regulated research involving children must comply with the requirements of 21 CFR 50, Subpart D and 21 CFR 56.

3.8.6.1. The IRB may waive the requirement to obtain parental permission, or to allow changes to, or omission of, some or all elements of this permission under circumstances that mirror those currently found in the Common Rule at 45 CFR 46.116(d) for research involving children that are covered by the FDA regulations. See *Policy and Procedures: Informed Consent Process for Research*.

3.8.7. For research supported by or intended for submission to the EPA (Environmental Protection Agency), the study must not involve the intentional exposure of children to any substance and requires compliance with 40 CFR 26 Subpart D for inclusion of children in observational research. See *WORKSHEET: Additional Federal Criteria*.

4. PROCEDURES: Researchers

4.1. The specific population/s that will be included and that may be considered as vulnerable must be identified in the submission.

4.1.1. The researcher must consider the setting of the research, procedures, and other permanent or temporary contexts that may affect a person's susceptibility to coercion or undue influence, comprehension, and risk of harm from procedures or loss of privacy.

4.1.2. Any additional information and assurances as prompted by specific pages in the submission pertaining to the identified vulnerable population must be provided.

4.2. Procedures must be identified as either for research/experimentation or as part of regular practice.

4.3. Special protections for the vulnerable population must be described where prompted in the submission.

4.3.1. Subjects involved in HIV-related research (HIV-infected persons and persons at risk of HIV-infection) are particularly vulnerable because of their disease status and because the disease disproportionately affects certain populations. An overriding concern in HIV research is confidentiality and privacy, since breaches of confidentiality could have severe adverse consequences. In ensuring that research adequately protects subjects' confidentiality, researchers should consider and address the following in the submission:

4.3.1.1. where identifiers are not required by the study design, they are not to be recorded;

4.3.1.2. if identifiers are recorded, they should be separated, to the greatest extent possible, from data and securely stored, with linkage restored only if necessary to conduct the research;

4.3.1.3. identifiers must be destroyed at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers;

4.3.1.4. if subjects will be given a fair and clear explanation of how information about them will be handled, including whether and how the information will be recorded in their medical records;

4.3.1.5. whether the protocol will specifically set forth how to respond to attempts to force disclosure of subjects' medical records or requests by third parties who have authorizations for disclosure signed by subjects; and,

4.3.1.6. whether the protocol will clearly state what information will be recorded, who is entitled to see records with identifiers, and whether any state laws require the reporting of HIV infection or the disclosure of other information.

4.3.2. In subjects with cognitive impairment, the researcher must describe the level of impairment and how this affects the individual's ability to provide informed consent.

4.4. If the research involves children:

4.4.1. The researcher must indicate the age of majority (adult status) corresponding to the location where research will be conducted.

4.4.2. The submission must include a description of the process for determining the age of participants in studies conducted via the Internet.

4.4.3. If the research includes enrollment of children in other countries, the researcher is responsible for providing the IRB with sufficient information to verify the age at which participants in such jurisdictions have the ability to consent to participation in research, including any medical treatments or procedures if applicable.

4.4.4. If the children are wards, the process to determine who is a guardian as it pertains to the location where research will be conducted must be described.

4.4.5. For studies supported by the U.S. Department of Education, parents must be provided with a way for parents to review instructional and/or data collection materials before agreeing to let their child participate. If the study involves collection of information concerning any of the following, signed parental permission will be required: political affiliations, mental and psychological problems potentially embarrassing to the student and his/her family, sex behavior and attitudes, illegal, anti-social, self-incriminating and demeaning behavior, critical appraisals of other individuals with whom respondents have close family relationships, legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers, or income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program). See the Protection of Pupil Rights Amendment (PPRA).

4.5. If the research includes adults who lack decision-making capacity, the submission must include a description of how capacity to consent will be assessed and, if applicable, how consent from a legally authorized representative will be obtained and how assent from the participant will be obtained. See *Policy and Procedures: Informed Consent Process*.

4.6. The researcher must identify applicable state law(s) regarding legal consent and legally authorized representative in the description of the consent process.

4.7. If the research involves sharing of results with the participants (e.g., HIV status or other incidental findings), the researcher should consider the circumstances under which participants should or must be informed of test results. The submission should include a description of the appropriate communication of results and, if applicable, available resources for counseling.

4.8. If a study is not approved for inclusion of prisoners and a participant is incarcerated while the study is ongoing, the researcher is responsible for notifying the IRB, and must either terminate the enrollment of the incarcerated participant or request for modification of the study to include the participant.

5. PROCEDURES: Institutional Review Board

5.1. The IRB will review the submission to determine if it involves vulnerable populations.

5.2. The IRB will determine if the study, any part of the study, or any study team member is funded or supported by a federal agency that has adopted the Common Rule.

5.3. The IRB will determine if the study involves the use of any FDA-regulated drug, biologic, or medical device.

5.4. The IRB determines if the inclusion of the vulnerable population is adequately justified and that safeguards are implemented to minimize risks unique to each population.

5.4.1. When appropriate, a Subject Matter Expert or ***Consultant*** will assist with the review.

5.4.2. If the study includes participants who may be considered vulnerable due to a temporary situation or the context of the study, the IRB will consider the participants as vulnerable and may require implementation of additional safeguards and protections for them.

5.4.3. If the study is not required to have or does not propose a data monitoring committee, the IRB should carefully review the data and safety monitoring plan to determine if a data monitoring committee is necessary.

5.4.4. Checklists pertaining to specific vulnerable populations must be completed and, where applicable, must contain protocol specific findings to support determinations.

5.5. During review, the IRB must determine which of the following categories will apply:

5.5.1. the research does not involve more than minimal risk to the subject;

5.5.2. the research is likely to benefit the subject directly, even if the risks are considered to be more than minimal;

5.5.3. the research involves greater than minimal risk with no prospect of direct benefit to individual subjects, but is likely to yield generalizable knowledge about the subject's disorder or condition; or

5.5.4. the research is not otherwise approvable but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of the subject.

5.6. IRB Staff will determine that additional federal agency criteria have been met for federally supported research using *WORKSHEET: Additional Federal Criteria* as a guide.

5.7. If the submission does not identify applicable state law(s) regarding legal consent and legally authorized representative, the IRB Staff will contact UGA OVPR legal counsel for assistance prior to approval by the IRB.

5.8. When reviewing a notification that a participant in an ongoing study has been incarcerated, the IRB should consider whether it is feasible for and in the best interests of the participant to remain in the study or to terminate enrollment.

5.8.1. If the study is federally funded but cannot meet the criteria for Subpart C, and the IRB determines it is in the best interests of the participant to remain in the study (e.g., for

health or safety reasons): 1) IRB staff will instruct the researcher to keep the participant enrolled, and 2) will inform OHRP of the decision along with the justification.

5.9. For ***non-committee reviews***, IRB staff will offer the investigator the opportunity to provide additional information/materials and/or to revise the submission in appropriate review correspondence.

5.10. For committee reviews, IRB staff will offer the investigator the opportunity to provide additional information/materials and/or to revise the submission in appropriate review correspondence that describes missing information or required modifications.

5.11. IRB Staff will document information pertaining to determinations that the requirements of this policy have been met in the review history for non-committee reviews and, for research reviewed by committee, in the meeting minutes by recording the motion to approve.

6. MATERIALS

6.1. WORKSHEET: Additional Federal Criteria
6.2. CHECKLIST: Children
6.3. CHECKLIST: Cognitively Impaired Adults
6.4. CHECKLIST: Neonates of Uncertain Viability
6.5. CHECKLIST: Non-Viable Neonates
6.6. CHECKLIST: Pregnant Women and Fetuses
6.7. CHECKLIST: Prisoners

7. REFERENCES

7.1. 45 CFR §46 Subpart A (Common Rule) and Subparts B-D
7.2. 21 CFR 50, Subpart D
7.3. 7.3. 21 CFR 56
7.4. 40 CFR 26 Subparts C and D
7.5. Policy and Procedures: Informed Consent Process for Research
7.6. Policy and Procedures: Exempt Review
7.7. Policy and Procedures: Review of Not Otherwise Approvable Research
7.8. Protection of Pupil Rights Amendment (PPRA), http://familypolicy.ed.gov/ppra

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07/17/2015: REV0 New Document
09/16/2016: REV1
01/18/2017: REV2
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