SOP

Department	Title	Dates
Research Integrity and Protection	Special Considerations for Vulnerable Populations	Effective: 2/19/2018
		Approved: 2/12/2018
SOP ID		Last Revised: n/a
IRB-SOP-906		Expiration: n/a

PURPOSE

This procedure explains and establishes the investigator and IRB responsibilities for ensuring additional protections are in place when involving vulnerable populations in research. DHHS regulations at 45 CFR 46.111(b), FDA regulations at 21 CFR 56.111(b), and the Common Rule require IRBs to give special consideration to protecting the welfare of particularly vulnerable subjects, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. The IRB is required to include adequate representation on the Board to consider specific kinds of research involving these vulnerable populations in a satisfactory manner.

SCOPE

This SOP applies to all research involving human subjects, or assist in the performance of such research activities, where that research is performed at or under the auspices of any Ascension Wisconsin system hospital or subsidiary ministry covered by and Ascension Wisconsin Federalwide Assurance for the Protection of Human Subjects (FWA).

DEFINITIONS

See SOP: Definitions (SOP-001)

PROCESS:

1. For all studies which fall under this SOP, the Investigator must complete IRB submission process, indicating any vulnerable populations that will be targeted for the research activities. The PI must include details about obtaining informed consent process and selection of participants with particular attention to preventing undue influence or coercion.

2. IRBs must pay special attention to specific elements of the research plan when reviewing research involving vulnerable subjects, including:
   - Strategic issues include inclusion and exclusion criteria for selecting and recruiting participants; informed consent and voluntarism; coercion and undue influence; and confidentiality of data.
   - The IRB should carefully consider group characteristics, such as economic, social, physical, and environmental conditions, so that the research incorporates additional safeguards for vulnerable subjects.
   - Investigators should not over-select or exclude certain groups based on perceived limitations or complexities associated with those groups. For example, it is not appropriate to target prisoners as research subjects merely because they are a readily available “captive” population.
   - Investigators must be knowledgeable about applicable laws that bear on the decision-making abilities of potentially vulnerable populations.
   - Research studies that plan to involve any potentially vulnerable populations must have adequate procedures in place for assessing subjects’ capacity, understanding, and informed consent or assent.

When weighing the decision whether to approve or disapprove research involving vulnerable subjects, the IRB will look to see that such procedures are a part of the research plan.

- In certain instances, it may be possible for researchers to enhance understanding for potentially vulnerable subjects. Examples include the inclusion of a consent monitor, a subject advocate, interpreter for hearing-impaired subjects, translation of informed consent forms into languages the subjects understand, and reading the consent form to subjects slowly to gauge their understanding paragraph by paragraph.

3. Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research

3.1. Research involving women who are or may become pregnant should receive special attention from the IRB because of women's additional health concerns during pregnancy and because of the need to avoid unnecessary risk to the fetus. Further, in the case of a pregnant woman, the IRB must determine when informed consent of the father is required for the research. Special attention is justified because of the involvement of a third party (the fetus) who may be affected but cannot give consent and because of the need to prevent harm or injury to future members of society.

3.2. Research Involving Pregnant Women or Human Fetuses. Pursuant to 45 CFR 46.204, pregnant women or human fetuses may be involved in research only if the study meets one of the three sets of criteria detailed in CHECKLIST: Research Involving Pregnant Women (CK-501).

3.3. In addition, Directive #51 of the Ethical and Religious Directives for Catholic Health Care Services states, "…nontherapeutic experiments on a living embryo or fetus are not permitted, even with the consent of the parents. Therapeutic experiments are permitted for a proportionate reason with the free and informed consent of the parents or, if the father cannot be contacted, at least of the mother. Medical research that will not harm the life or physical integrity of an unborn child is permitted with parental consent."

3.4. Research Involving Neonates. Pursuant to 45 CFR 205, neonates of uncertain viability may be involved in research only if the study meets one of the two sets of criteria detailed in CHECKLIST: Research Involving Neonates of Uncertain Viability (CK-701).

3.5. Research Involving Nonviable Neonates. Pursuant to 45 CFR 46.205, after delivery, a nonviable neonate may not be involved in research unless all of the criteria detailed in CHECKLIST: Research Involving Non-Viable Neonates (CK-601).

3.6. Pursuant to 45 CFR 46.206, 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. **In accordance with the Ethical and Religious Directives for Catholic Health Care Services, human tissue obtained by direct abortions may not be used.** If information associated with the 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 subparts of this part are applicable.

4. Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects

4.1. Because prisoners may not be free to make a truly voluntary and un-coerced decision whether or not to participate as subjects in research, the regulations require additional safeguards for the protection of prisoners in research. These safeguards apply to all research that includes any individual who is or becomes a prisoner while participating in a research study. The IRB must consider the kind of research, and risks and benefits of the study to ensure the equitable selection of research subjects and that the possibilities of coercion or undue influence are minimized.

4.2. Pursuant to 45 CFR 46.306, biomedical or behavioral research may involve prisoners as subjects only if the IRB determines that the proposed research meets one of two criteria detailed in CHECKLIST: Research Involving Prisoners (CK-801).

4.3. <u>Unexpected Incarceration of an Enrolled Subject</u>

4.3.1. If a human subject involved in ongoing research becomes a prisoner during the course of the project, and the research proposal was not reviewed and approved by the IRB in accordance with Subpart C of 45 CFR part 46, the investigator must promptly notify the IRB

4.3.2. All research interactions and interventions with the now-incarcerated prisoner-subject, or their identifiable private information, must cease until all of the requirements of subpart C of the DHHS regulations have been satisfied with respect to the relevant protocol. In special circumstances in which the principal investigator asserts that it is in the best interests of the subject 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.

4.3.3. The subject does not have to be formally withdrawn; as long as there is no interaction, intervention or obtaining data with the subject while incarcerated (see above) subpart C is not invoked. Therefore, there is no need to withdraw and re-enroll. If the investigator can wait until the person is no longer incarcerated, subpart C is never an issue.

4.3.4. Data that had been acquired prior to incarceration may continue to be analyzed.

4.3.5. If the investigator wishes to have the prisoner subject continue to participate in the research, the convened IRB will re-review the change to the research protocol in a timely manner and in accordance with the requirements of subpart C, to ensure that the rights and wellbeing of the now-incarcerated prisoner subject are not in jeopardy.

4.3.6. The convened IRB should evaluate if the now-incarcerated prisoner-subject can continue to consent to participate, is capable of meeting the research protocol requirements, the terms of the now-incarcerated prisoner-subject's confinement does not inhibit the ethical conduct of the research, and there are no other significant issues preventing the research involving human subjects from continuing as approved.

4.3.7. The IRB can either: (a) approve the involvement of the Prisoner-subject in the research in accordance with this policy; or (b) determine that this subject must be withdrawn from the research.

4.3.8. The institution(s) engaged in the research involving the prisoner subject must send a certification to OHRP and wait for a letter of authorization in reply.

5. Additional Protections for Children Involved as Subjects in Research

5.1. The special vulnerability of children makes consideration of involving them as research participants particularly important. To safeguard their interests and to protect them from harm, special ethical and regulatory considerations apply for reviewing research involving children.

5.2. Pursuant to 45 CFR 46, Subpart D and 21 CFR 50, Subpart D, the IRB can approve research involving children as research subjects only if the study meets the criteria detailed in CHECKLIST: Research Involving Children (CK-901).

6. Additional Protections for Individuals with Cognitive Impairment.

6.1. In the absence of evidence to the contrary, the law assumes competence in adults. However, certain groups of individuals may be suspected of lacking competence. These include persons with mental retardation/developmental disability, dementia, delirium, or major psychiatric disorders, such as schizophrenia. Patient groups that are susceptible to decreased competency include the elderly, terminally ill, and neurology patients. Patients on certain medications may also suffer a lack of competence. Conversely, the presence of cognitive impairment does not automatically disqualify a subject from consenting/assenting to or refusing research participation. The critical issue is whether the cognitive impairment leads to an impaired decisional capacity.

6.2. Assessment of Competence in Potential Research Subjects. There are no well-established, standardized measures for determining competency to consent to research. Therefore, assessment should be done on an individual basis and should determine the ability of the potential subject to:

- understand the nature of the research and of his/her participation
- appreciate the consequences of the participation

- show the ability to consider alternatives, including the option not to participate
- show the ability to make a reasoned choice
- Investigators must not interpret the potential subject's attentiveness and agreeable comments/behavior as evidence of the potential subject's competence or willingness; many cognitively impaired persons retain attentiveness and social skills.
- The IRB can approve research involving cognitively impaired adults if the study meets the criteria detailed in CHECKLIST: Research Involving Cognitively Impaired Adults (CK-1001).

7. Additional Protections for Associates/Employees/Affiliated Staff or Physicians (including trainees) as research subjects

7.1. Employees, Associates, and Affiliated Staff (e.g., full-time, part-time, temporary, visiting, medical students, residents, fellows, etc.) may be recruited for research participation; however, an employee/associate/affiliated staff shall not be required to participate in research or as a condition of employment. Employees/associates/affiliated staff should not be selected solely on the basis of convenience.

7.2. Recruitment of potential participants who are employees/associates/affiliated staff must be designed to minimize the possibility of coercion or undue influence. Potential participants should not be solicited from individuals who report directly to the investigator(s). To avoid potential influence when recruiting employees and ensure voluntary participation, the investigator(s) should develop recruitment strategies that create a barrier between the managerial and employee relationships.

7.3. The informed consent must disclose to potential participants that protecting the confidentiality of research participants' personal information may present challenges that may not be guaranteed. Protecting the confidentiality of research participants' personal information when the participants are employees/associates/affiliated staff may also present additional challenges. The extent to which medical information and/or research data may be accessible to supervisors or others not directly involved in the research must be considered and disclosed to potential participants in the informed consent process.

7.4. Research which targets the enrollments of employees/associates/affiliated staff (including students, residents, fellows, and other trainees), where the research will be conducted requires:
- Record of participation or non-participation may not be linked to employment record.
- Employees, residents, fellows and trainees may not be directly recruited by their supervisor.
- Research which enrolls employees/associates/affiliated staff must obtain approval from the appropriate department manager/director prior to seeking IRB review and approval. Such departmental approval must be reflected in the IRB submission documentation.

7.5. Research which involves students 18 years or younger will be reviewed as research involving children.

8. Additional Protections for Students/Athletes at Academic Institutions

8.1. Research which targets the enrollments of students/athletes at academic institutions (including K-12 schools) requires:
- Record of participation or non-participation may not be linked to academic record.
- Students will not be directly recruited by an individual for whom the student my perceive coercion to participate in the research (e.g. instructor, coach, sports trainer, etc.)

8.2. Research which involves students/athletes 18 years or younger will be reviewed as research involving children.

9. Additional Protections for Other Vulnerable Populations

9.1. Although federal research regulations cover specific vulnerable groups, there are other potentially vulnerable groups beyond those discussed above. For all vulnerable populations, Federal regulations require that the IRB ensures that "additional safeguards [are] included in the study to

protect the rights and welfare" of all subjects that are "likely to be vulnerable to coercion or undue influence."

9.2. Examples of populations that the IRB may consider vulnerable include the following: non-English speaking populations, educationally or economically disadvantaged, nursing home residents, individuals with life-threatening condition or seriously debilitating illness, members of the military, minority groups, or homeless or refugees.

9.3. An investigator who intends to include any possibly vulnerable population in research must provide sufficient detail in the research protocol regarding the plan for inclusion, including the plan for obtaining informed consent and HIPAA Authorization (if applicable) and any other additional provisions during the study. The IRB will review the potential risks and benefits of each proposed study on a case-by-case basis to assure rights and welfare are protected, coercion is minimized, and the study is conducted with the utmost regards for ethical standards.

REFERENCES:

- 45 CFR 46
- 21 CFR 56
- Ethical and Religious Directives for Catholic Health Care Services, 5th Edition (2009)

RELATED MATERIAL

- SOP: Research Involving Subjects with Limited English Proficiency (SOP-909)
- SOP: Research Involving Children (SOP- 908)
- SOP: Research Involving Adults with Decreased Decision Making Ability (SOP-907)
- CHECKLIST- Research Involving Pregnant Women (CK-501)
- CHECKLIST- Research Involving Non-viable Neonates (CK-601)
- CHECKLIST- Research Involving Neonates of Uncertain Viability (CK-701)
- CHECKLIST- Prisoners (CK-801)
- CHECKLIST- Children (CK-901)
- CHECKLIST- Research Involving Cognitively Impaired Adults (CK-1001)

REVISION HISTORY

Version #	Date Revised	Reason for/Brief Description of Change	Revised By
01	11/27/2017	New- Initial Integration Update	J. Blundon