TITLE: Institutional Review Board Special Considerations
SC 500 Research Involving Potentially Vulnerable Subjects

ORIGINATOR: IRB Chairperson

APPROVAL: IRB Chairperson

POLICY STATEMENT: Research involving potentially vulnerable populations warrants additional safeguards. The IRB will require researchers to use appropriate safeguards to protect rights and welfare of these participants if it determines that they may be vulnerable to coercion or undue influence. The IRB will review protocols that include participants that are potentially vulnerable to coercion or undue influence and will take extra precautions to ensure appropriate safeguards are in place to protect the participants from potential harm. The IRB must consider whether the welfare and safety of all individuals are adequately protected. Unlike research involving children, prisoners, and individuals with impaired decision making capacity, no additional Department of Health and Human Services (DHHS) regulations specifically govern research involving other persons who may be considered vulnerable.

Exclusion or inappropriate representation of groups of individuals may impact the study outcome's generalizability. While the potential for being vulnerable should not prevent participation in research, it is important to keep in mind that additional scrutiny is warranted for research involving populations such as those who may be considered economically or educationally disadvantaged, minority groups, terminally ill and Non-English speaking. In addition to federal regulations, all research conducted at Mercy Health regional sites, comply with the CHE Trinity Health Mission, Core Values, and Catholic moral/ethical principles, as delineated in the "Ethical and Religious Directives for Catholic Health Care Services." In this regard, IRB review and decision making gives special consideration for research participants' cultural, racial, social, religious, and economic circumstances.

GENERAL PROVISIONS:
Researchers must include in their proposals sufficient justification for inclusion of participants who are potentially vulnerable and they must provide a written plan to protect them and their surrogates from coercion and undue influence. The IRB will determine whether the involvement of such individuals in research is justified and determine whether the proposed plan minimizes or eliminates the risks to vulnerable subjects. The IRB will consider additional safeguards to protect participants. In order for potentially vulnerable individuals to be ethically enrolled in research, Investigators and IRBs should consider ways to enhance subjects' understanding of information relevant to the consent process, in a manner that is consistent with the common rule and the ethical principles outlined in the Belmont Report. When the IRB reviews research that involves categories of participants vulnerable to coercion or undue influence, the review process will include one or more individuals who are knowledgeable about or experienced in working with these participants. The IRB will also take into account, and expects investigators to take into account, subjects' abilities, impairments and needs when considering whether to invite these populations to participate in research. Such decisions may be based on the amount of risk involved in the research and the likelihood that participants will derive health benefits from their participation.
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participation. They may include: 1) requiring involvement of participant advocates 2) requiring independent monitoring 3) requiring waiting periods or providing information incrementally 4) appointing a monitor to supervise the informed consent process.

The IRB considers the following elements of the research plan when reviewing research involving vulnerable participants:

- **Strategic issues**
  Inclusion and exclusion criteria, informed consent, coercion and undue influence; and confidentiality of data

- **Group characteristics**
  Economic, social, physical, and environmental conditions

- **Participant selection**
  To prevent over-selection or exclusion of certain participants

**Safeguards to Minimize Coercion or Undue Influence**

- Care must be taken to ensure participants' incentives for research participation are commensurate with the risks, discomforts and inconveniences involved in the research, and financial or other gains are not overly compelling.

- Recruitment materials may not promise "free" treatment or emphasize the medical care that participants may receive during the research.

- Recruitment processes occurring in institutional or other controlled settings must be carefully designed to ensure participation is truly voluntary.

- To ensure equity in enrollment, other factors bear consideration when planning research for persons who are economically disadvantaged (e.g., costs for child care or transportation).

- Individuals or populations that might be temporarily or permanently vulnerable include, but are not limited to, those who:
  1) Are susceptible to coercion or undue influence (e.g., the homeless, prisoners, students, patients with limited or no treatment options, socially and economically disadvantaged).
  2) Lack comprehension of the research and its risks (e.g., educationally disadvantaged, dementia, schizophrenia, or depression).
  3) Have increased susceptibility to harm from the procedures of the specific study under review (e.g., individuals who would have to answer study survey questions about their sexual assault).
  4) Are at risk for economic, social, or legal consequences from the study (e.g., individuals who would have to answer study survey questions about their drug use or HIV status).
  5) Have impaired capacity to consent (progressive, fluctuating or permanent).

**CONSENT**

In general, all adults, regardless of diagnosis or condition, should be presumed competent to consent to participation in research unless there is evidence of serious disability that would impair reasoning or judgment. For those individuals who may fall into the category of having impaired decision making capacity, please refer to
IRB SOP SC 502. Adult subjects should read and sign the informed consent document in the standard manner unless a waiver or alteration of the informed consent process or documentation has been granted by the Mercy Health Regional IRB.

A. Non-English Speaking

Informed consent must be obtained in a language understandable to the participant. If participants who are not fluent in English are to be recruited, the investigator must involve individuals who can speak the appropriate language and conduct the consent discussion. Consent forms will also need to be translated into the appropriate language at the same reading level as the English versions. Translations of the informed consent document are the responsibility of the Principal Investigator and/or study sponsor. Costs for translation should be considered during study budget planning. The documents may be either a standard consent form or “short-form consent.” When the person obtaining consent is assisted by an interpreter, a translator or second interpreter should also be present during that conversation, the second translator or interpreter may serve as the witness.

The IRB may review these documents with outside experts to ensure that the translation is appropriate.

1. Consent should always be obtained in the native language of the participants. A consent form or oral consent script in the participant’s native language and an English translation must be provided to the IRB.

2. When the IRB reviews research that involves non-English speaking participants, the IRB considers:
   a. Whether the enrollment of non-English speaking participants is justified by the research questions.
   b. Whether recruitment and consent documents are translated into the native language of participants.
   c. Whether the individuals communicating information to the participant or the representative during the consent process will provide that information in language understandable to the participant or the representative.

B. Illiterate Participants

Participants known to be illiterate should be provided with an opportunity to involve a study partner who can confirm the consistency of written consent materials and other documents that will need to be provided to the participant orally. When written documentation of informed consent is required, a short form consent may be used or a witnessed informed consent form where the witness’s signature attests to the information having been provided to the participant in a format understandable to the participant, such as orally.

C. Economically Disadvantaged

Economically disadvantaged individuals may be easily coerced with incentives. They also may not otherwise have access to health care.

D. Educationally Disadvantaged

Educationally disadvantaged individuals may have issues understanding the informed consent process. Illiteracy may prevent them from doing surveys or from performing written instructions. It may not be apparent that an individual is educationally disadvantaged; therefore, the researcher needs to be aware of their subject’s circumstances.
E. **Minorities**

Federal regulations governing research with minorities, *per se*, have not been adopted. Nevertheless, IRBs are required to include additional safeguards in studies where "some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as... economically or educationally disadvantaged persons". Research plans should provide sufficient information about the racial and ethnic composition of the study population to outline minority representation. Women and members of minorities groups and their subpopulations should be included in research, unless a clear and compelling rationale and justification that inclusion is inappropriate with respect to the health of the individuals or the purpose of the research. Women of child bearing potential should not be routinely excluded for participation in research.

F. **Elderly & Aged Individuals**

The IRB considers elderly as 65 years of age and older. It is generally agreed that the elderly are not usually in need of special protections, except in two circumstances: cognitive impairment and institutionalization. Under those conditions, the same considerations are applicable as with any other, nonelderly subject in the same circumstances. In the past, persons in nursing homes or other institutions have been selected as subjects because of their easy accessibility. It is now recognized, however, that conditions in institutional settings increase the chances for coercion and undue influence because of the lack of freedom inherent in such situations. The IRB will take into consideration the environment and location of subject recruitment when elderly persons are recruited for research purposes. It is also important to note elderly persons may have hearing or vision problems and may therefore require more time to have the study explained to them. The use of age as the criterion to consent and therefore participate in research is not valid. The IRB must take into account that despite there potentially being some impairment to competence, potential participants can make reasonable choices to participate.

G. **Terminally Ill Individuals**

Severe illness often affects a person's competence, and terminally ill patients may be vulnerable to coercion or undue influence because of a real or perceived belief that participation is necessary to receive continuing care from health professionals or because the receipt of any treatment is perceived as preferable to receiving no treatment. Two important reasons for concern regarding research involving terminally ill persons are: (1) they tend to be more vulnerable to coercion or undue influence than healthy adult research subjects; and (2) research involving the terminally ill is likely to present more than minimal risk. While it is generally considered unacceptable to have such persons participate in research it may be necessary to involve terminally ill patients in research concerning their specific disease and treatment.

H. **Mentally Ill**

The predominant ethical concern in research involving individuals with psychiatric, cognitive, or developmental disorders, or who are substance abusers is that their disorders may compromise their capacity to understand the information presented and their ability to make a reasoned decision about participation. Many individuals with disabilities affecting their reasoning powers may be residents of institutions responsible for their total care and treatment. The impact of institutionalization may further compromise their ability to exercise free choice (voluntariness). These concerns apply both to voluntary patients and those committed involuntarily. The eagerness for release may induce an institutionalized person, especially one who is involuntarily confined, to participate in research out of a desire to appear "rational" and "cooperative" to those who will make decisions about his or her release. It is important to take prospective participants' abilities, impairments, and needs into account when considering whether to invite them to participate in research.

In addition, IRB members should also consider the following:

- Sufficient justification for using that population.
- Are noninstitutionalized subjects appropriate for the research and reasonably available?
- Does the research pertain to aspects of institutionalization?
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- Are adequate procedures proposed for evaluating the mental status of prospective subjects to determine whether they are capable of consenting? Are these procedures appropriate both to the subject population and the nature of the proposed research?
- Is more than minimal risk involved? If so, is the risk justified by anticipated benefits to the participating subjects and the importance of the knowledge that may reasonably be expected to result?
- Is it possible to identify persons authorized to give legally valid consent on behalf of any individuals judged incapable of consenting on their own behalf? Should assent of the prospective subjects also be required? If incapable of giving valid consent, can subjects' objection to participation be overridden? Under what circumstances?
- Should an advocate or consent auditor be appointed to ensure that the preferences of potential subjects are elicited and respected? Should someone ensure the continuing agreement of subjects to participate, as the research progresses?
- Should the patient's physician or other health care provider be consulted before any individual is invited to participate in the research? Is the research likely to interfere with ongoing therapy or regimens? Is it possible that the request to participate itself might provoke anxiety, stress, or other serious negative response?

REFERENCES:
45 CFR 46.111
45 CFR 46.107
45 CFR 46, Subparts B–D
21 CFR 56.111
OHRP IRB Guidebook: Chapter VI – Special Classes of Subjects
http://www.hhs.gov/ohrp/archive/irb/irb_chapter6.htm#gt
World Medical Association Declaration of Helsinki: ethical principles for clinical research involving human subjects. WMA 2002
http://www.irb.vt.edu/pages/elderly.htm
https://kb.wisc.edu/hsirbs/page.php?id=27051

ATTACHMENTS:
SC 500-A Research Involving Vulnerable Subjects Worksheet

PROCEDURE: All Mercy Health Campuses

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<th>Responsibility</th>
<th>Action</th>
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<tr>
<td>IRB Specialist/IRB Coordinator</td>
<td>1. Verifies that the protocol submission documents are complete and contain sufficient information on safeguards for research involving potentially vulnerable participants for the IRB to review.</td>
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<td>2. Reviews, specifically, informed consent documents for consent, assent and permission for LAR, as applicable.</td>
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<td>3. Ensures the minutes reflect the deliberations of the IRB regarding any decisions rendered.</td>
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<td>4. Ensures the IRB letter includes the proper language referencing the findings and directives of the IRB.</td>
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IRB Chairperson or Designee

1. Reviews protocol at time of initial and continuing review, and review of modifications to determine if the group of individuals that are being asked to participate will include those with potentially vulnerable participants.

2. Guide discussion and reviews considering the need for additional protections for individuals who are potentially vulnerable as outlined in 45 CFR 46.111(a) (3): “Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons.”

For Expedited Review:

1. Takes into account the individuals targeted for the study population.

2. Determines that adequate provisions for obtaining consent and/or assent or waiver of assent from the participant are addressed and also how documentation of consent will be noted.

3. Reviews and determines if the method of screening potential participants is acceptable. Reviews the reasoning and factors for excluding potential participants from the study.

4. May recommend additional safeguards for the participants in order to secure approval of the research.

5. If unable to approve the research, forwards for convened IRB review.

IRB Members/IRB Designated Reviewers

1. Utilizing the IRB Review Worksheet as assigned, reviews the submission documents in accordance with criteria for approval with 45 CFR 46.111 and 21 CFR 56.111 if applicable, and other applicable regulations.

2. When additional expertise is required, may request a consultant to assist with review for additional safeguards in potentially vulnerable populations.

3. Recommend additional safeguards to protect the rights and welfare of individuals who are potentially vulnerable as appropriate.

4. Determine and document that the informed consent process for consent, assent and permission of the participant, minimizes possibility of undue influence and coercion.

Principal Investigator

1. Carefully consider the population being recruited for participation in the study. If the population is a potentially vulnerable population, provide sufficient justification and a written plan to protect them and their surrogates from coercion and undue influence.