POLICY STATEMENT: Individuals without decision-making capacity are a vulnerable population in research, and research involving these subjects warrants additional safeguards. Research involving these populations frequently presents greater than minimal risk, may not offer direct medical benefit to the subject, and may include a research design that calls for washout, placebo or symptom provocation. The IRB will require researchers to use appropriate safeguards to protect rights and welfare of these participants and those providing consent on their behalf if it determines that they may be vulnerable to coercion or undue influence. The IRB will review protocols that include participants with impaired decision making capacity to ensure appropriate safeguards are in place to protect the participants from harm. Unlike research involving children, prisoners, pregnant women, and fetuses, no additional Department of Health and Human Services (DHHS) regulations specifically govern research involving persons who are cognitively impaired. While limited decision-making capacity should not prevent participation in research, it is important to keep in mind that additional scrutiny is warranted for research involving this population. In addition to federal regulations, all research conducted at Mercy Health regional sites complies 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 lack decision-making capacity and a 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. 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. They may include: 1) requiring involvement of participant advocates, 2) requiring independent monitoring, 3) requiring waiting periods, 4) appointing a monitor to supervise the informed consent process.

In accordance with federal regulations, where an adult individual is unable to consent to participate in research for themselves, consent may be obtained from that individual's legally authorized representative. For purposes of research conducted at Mercy Health, a legally authorized representative is an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. Usually "the law of the jurisdiction in which the research is conducted" will be the state law where the research procedures will be performed.

Although not specifically addressed in the regulations as a vulnerable population, the Mercy Health IRB requires additional safeguards for research involving persons with decisional impairment.

The IRB will approve the research only if it finds that:
1. The research bears a direct relationship to the decisionally impaired subject's condition or circumstance;
2. The research meets one of the following criteria:
   • presenting no greater than minimal risk to the involved subjects;
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- presents an increase over minimal risk to involved subjects, but which offers the potential for direct individual benefit to the subject;
- presents a minor increase over minimal risk to involved subjects and which does not have the potential for direct individual benefit; provided that the knowledge sought has direct relevance for understanding or eventually alleviating the subjects’ disorder or condition.

In evaluating a protocol involving the enrollment of persons with decisional impairment, The IRB may consider requiring additional safeguards, as appropriate, for a given protocol. Such safeguards may include any of the following:
- Use of an independent party (independent of the study investigator with appropriate expertise) to assess the capacity of the potential subject;
- Use of standardized assessment of cognition and/or decisional capacity;
- Use of informational or educational techniques;
- Use of an independent person to monitor the consent process;
- Use of waiting periods to allow for additional time to consider information about the research study;
- Use of proxy consent;
- Use of assent in addition to proxy consent in order to respect the autonomy of individuals with decisional impairment.

ASSESSING CAPACITY TO CONSENT
There are no generally accepted criteria for determining competence to consent to research for persons whose mental status is uncertain or fluctuating so the role of the IRB in assessing the criteria proposed by the investigator is of major importance. Both IRBs and clinical investigators must keep in mind that decision making capacity may fluctuate, requiring ongoing assessment during the course of the research. The consent process should be ongoing. The IRB, at its discretion, may require an outside witness to observe the consent process.

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.

In making the determination about whether it is appropriate for investigator’s to utilize proxy consent, the IRB will take into consideration the following:
- The rationale for the need to obtain proxy consent;
- The criteria that will be used in determining whether a potential subject has decisional impairment sufficient to require the use of proxy consent, including any use of standardized assessment tools;
- Whether any additional methods are proposed to enhance subjects’ ability to achieve decisional capacity with regard to the proposed study (e.g., reading of the consent form may not be sufficient and use of other tools such as videos, educational materials, post-test, etc. might be considered to assist potential subjects in understanding what is involved with the research);
- Who will be approached, and in what order, to provide proxy consent.

The following are specific procedures that must be followed if proxy consent is utilized:
- Persons with decision impairment may also have been adjudicated legally incapacitated by a court decision. If such persons are considered for enrollment in a research protocol, the only party who may provide proxy consent is the court-appointed guardian. The guardian may only provide proxy consent if the court order, appointing them guardian, specifically states that they have the authority to enroll the incapacitated person into a research protocol. For this category of subjects, a copy of the court order appointing the guardian and granting the guardian authority to enroll the person into a research study should be attached to the informed consent document.
- Persons may also, through a health care proxy appointed by a power of attorney, designate a person to make decisions for them in the event that they are subsequently incapacitated. This person may give proxy consent for enrollment of a subject in research.
- If a potential subject has neither a guardian, nor a health care proxy designated, the investigator may obtain the informed consent of the subject’s legally authorized representative. Legally Authorized Representative (LAR): An individual who is authorized under the law of the state to consent to research on behalf of someone who is cognitively impaired and unable to comprehend the consent. Such consent may be obtained from a health care agent appointed by the person in a Durable Power of Attorney for Healthcare (DAHC) or similar document; court-appointed guardians for the person, or from next of kin in the following order of priority, unless otherwise specified in applicable law:
  - Spouse;
  - natural or adoptive parent;
  - adult child;
  - adult brother or sister;
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- any other available adult relative related through blood or marriage known and documented to have made decisions for the subject in prior health care settings.

When a person is giving proxy consent, the proxy should be informed that, where possible, s/he should base the decision on substituted judgment, reflecting the views that the subject expressed while decisionally capable. The proxy should be fully informed on the risks, benefits and alternatives to the research. If the values of the subject are not known with respect to a proposed research study, the proxy should act in the best interest of the subject.

If a person with decisional impairment is capable of exercising some judgment concerning the nature of the research and participation in it, the investigator should obtain the subject’s assent in addition to the consent of his/her legally authorized representative.

The verbal objection of an adult with decisional impairment to participation in the research should be binding. If the subject, at any time, objects to continuing in the research study, such objection should be respected.

Where the condition causing the subject’s decisional impairment is of an intermittent or temporary nature, the informed consent process should include a mechanism for obtaining the subject’s subsequent direct informed consent to participate in the research. If a subject regains decision making capacity and declines to continue in the research, the decision must be respected.

COMPREHENSION

The determination of a subject’s ability to understand the implications of the decision to participate in research is best made by the investigator. There is no universally accepted test or standard for making a determination of comprehension. This process should operate in research studies in much the same manner as the informed consent process in clinical treatment that does not involve research.

DOCUMENTATION OF CONSENT AND ASSENT: INFORMED CONSENT DOCUMENT

Adult subjects, not deemed to have decisional impairment, should read and sign the informed consent document in the standard manner.

For adult persons with decisional impairment, the investigator should document the following before obtaining the consent and signature of the subject’s legally authorized representative or guardian and the signature of the witness to this consent:

- the conclusion that the subject is incapable of understanding the information presented regarding the research, to appreciate the consequences of acting (or not acting) on that information, and to make a choice;
- the information provided to the subject’s legally authorized representative regarding the cognitive and health status of the subject, the risks and benefits of the research, and the role of the proxy.

To document obtaining the assent of a subject with decisional impairment, a Verification of Explanation statement should appear on the consent document and be signed and dated by the Principal Investigator, listed co-investigator, or other research staff when authorized by the IRB.

The ability of individuals to participate in research if they are unable to consent depends on the law of the state where the research is being conducted. If the site of the research is outside Michigan, the researcher must provide a legal opinion acceptable to the IRB of the circumstances under which the law of the state where the research is conducted allows individuals who do not have the capacity to consent to participate in research. Also, the IRB or investigator may seek advice from Mercy Health Risk Management Department on the definition of a legally authorized representative for the applicable jurisdiction.

DOCUMENTATION OF CONSENT AND ASSENT: RESEARCH RECORD

In studies in which some or all participants may have decisional impairment, it is recommended that at the time of obtaining consent the following be documented in a note to file for the subject’s research record:

- Whether the subject demonstrated the ability to understand the nature of the research procedures, the potential risks and benefits, the voluntary nature of the participation and to make a personal judgment about participation;
- Use of any supplemental methods to enhance or evaluate decisional capacity;
- A summary of the matters discussed with the subject’s legally authorized representative.

DEFINITIONS:

- Decisionally impaired persons are those who have a diminished capacity to understand the risks and benefits for participation in research and to autonomously provide informed consent. This decisional impairment may result from a psychiatric, organic, developmental or other disorder that affects cognitive or
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emotional functions, or may result from the effect of drugs or alcohol. The impairment may be temporary, 
permanent or may fluctuate.

- Legally Authorized Representative: An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject’s participation in the procedure(s) involved in the research.

REFERENCE:
45 CFR 46.111
21 CFR 56.111

ATTACHMENTS:
502-A Worksheet: Research Involving Decisionally Impaired Adults

PROCEDURE: All Mercy Health Campuses

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| IRB Clinical Research Assistant/IRB Coordinator | 1. Verifies that the protocol submission documents are complete and contain sufficient information on safeguards for decisionally impaired participants for the IRB to review.  
2. Reviews, specifically, informed consent documents for consent, assent and permission for LAR, as applicable.  
3. Ensures the minutes reflect the deliberations of the IRB regarding any decisions rendered.  
4. Ensures the IRB letter includes the proper language referencing the findings and directives of the IRB. |
| IRB Chairperson                     | 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 impaired decision making capacity.  
2. Using IRB Review Worksheet as a discussion guide, reviews additional protections for individuals without decision-making capacity, 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, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons.” |

For Expedited Review:
1. Takes into account the decision-making capacity of the participants 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 and controls and the factors that will be the basis for excluding potential participants from the study (e.g., mini-mental status exam or instrument to demonstrate capacity to consent) are adequate.
4. May recommend additional safeguards for the decisionally impaired participants in order to secure approval of the research.
5. If unable to approve the research, forwards for convened IRB review.

IRB Members

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 decisionally impaired participants.
3. Makes the following specific findings and determinations (may apply to all participants involved in the study, or on a case-by-case basis, as deemed necessary by the IRB):
   - The research is intended to study a disease or condition relevant to the vulnerable participant,
   - Procedures adequately account for the degree and variability of intellectual impairment,
   - Anticipated direct benefits to the participant, if any,
   - The level of risk is commensurate to the benefits, and
   - Provisions for both the assent of the participant and the permission of a legally authorized representative are adequate.
4. Recommends additional safeguards to protect the rights and welfare of individuals without decision-making capacity, as appropriate.
5. Determines and documents that the informed consent process for consent, assent and permission of LAR, as applicable, minimizes possibility of undue influence and coercion.
6. May determine that an enrolled participant without decision-making authority should receive information or provide informed consent during the research study if he/she later regains decision-making capacity.