MCW Office of Research
Standard Operating Procedure

RESEARCH WITH SUBJECTS LIKELY TO MANIFEST OR DEVELOP DECREASED DECISIONAL ABILITY

Unit: Human Research Protections Program (HRPP), Office of Research
Applies to: MCW/FH Faculty and Staff involved in human research

PURPOSE:
Federal regulations and the MCW IRB require that subjects provide written consent prior to their involvement in human subjects research, unless the IRB has approved a waiver of consent procedures per 45 CFR 46.116(c)(d) or 45 CFR 46.101(i). In the event that an adult lacks capacity to consent, Federal regulations require that informed consent is obtained from a legally authorized representative.

MCW IRB considers subjects who have or are likely to develop decreased decisional abilities as a vulnerable population. 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.”

This document outlines institutional requirements, and provides guidance to MCW/FH faculty and staff who may wish to engage in research with subjects who currently have decreased decisional ability or are likely to develop decreased decisional ability in the future.

DEFINITIONS:
Legally Authorized Representative (LAR) - “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” (45 CFR 46.102 (c)) (21 CFR 50.3 (1)). Note that applicable law varies from state to state within the United States.

Consent - refers to an explicit agreement to participate in a certain action, particularly and especially after thoughtful consideration.

Assent – an affirmative agreement to participate in research. Absence of disagreement to participate does not imply agreement to participate in research.

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.

Decreased Decisional Ability - Persons who evidence decreased ability to understand, reason, and/or decide. The impairment may be due to disorders of a psychiatric, organic (including those suffering from delirium or degenerative brain diseases), developmental
(e.g., mental retardation), substance misuse (e.g., those under the influence of or
dependent on drugs or alcohol), or other nature that affects cognitive or emotional
functions. Trauma patients, for example, may transiently lack decisional ability due to
debilitating pain, taking medication to relieve debilitating pain, having strong medication
side effects, or having trouble communicating.

**Qualified assessor** – Trained professional who provides an assessment of a subject’s
decisional ability. A qualified assessor can be a member of the study team and/or
associated with the conduct of the study who also possess the necessary skills, abilities,
clinical expertise, and education specific to the disease or disorder being studied and
who also has a good understanding of the informed consent process.

**Independent assessor** – Qualified trained professional who provides an assessment of
a subject’s decisional ability. An independent assessor is not associated with the
conduct of the study. The independent assessor should not be included as an author on
any presentation or publication reporting on the study.

**PROCEDURE:**

For research involving adult subjects with mental illnesses or cognitive impairments, the
Investigator(s) must be knowledgeable about the relevant disorders and the range of
impairment likely to be present in the subject population. In their IRB applications,
Investigators must propose specific research safeguards for individuals with current or
potential to develop decreased decisional ability. These safeguards and protections
should be proportional to the degree of decisional impairment, the magnitude of the
experimental risk, or both.

Investigators typically encounter two situations in their research which require a plan and
safeguards for involving subjects with decreased decisional abilities:

- Research involving subjects who lack the ability to provide informed consent at
  the time of initial recruitment to the study, and
- Research involving subjects who are currently deemed decisional, but who may
  progressively lose their decisional ability due to their underlying condition (such
  as Alzheimer’s disease) and the duration of the study.

When the subject lacks decisional ability, the Investigator must obtain informed consent
from a legally authorized representative, and also obtain and document the assent of the
subject to participate whenever possible.

For research involving progressive disorders (such as Alzheimer’s) or aging populations,
subjects may be competent to consent on their own behalf at the beginning of the study,
but their condition may change or deteriorate over the course of the study. When a
subject in an ongoing study loses his/her decisional ability (transiently or irreversibly),
the subject’s participation in the study must be considered ended until a legally
authorized representative has consented to continuation on behalf of the subject.

To anticipate these kinds of situations, and to facilitate decisions consistent with the
subject’s wishes, Investigators should consider the following measures at the very
beginning for subjects who may lose their decisional ability over the course of a study,
but are still capable of consent:

- discuss whether the prospective subject would want to continue study
  participation after becoming decisionally impaired, and document any wish to
  continue;
identify the subject's legally authorized representative (LAR) according to applicable state law and the IRB procedure entitled "Legally Authorized Representatives (LARs): Who Can Consent to Research on Behalf of an Adult Subject with Decreased Decisional Ability?", involve the LAR in the initial consent process, and provide the LAR with documentation of the subject's wish to continue participation after becoming decisionally impaired.

For most studies, informed consent should not be elicited and documented on the same day that the subject is first presented with information about the study. This principle is particularly important for studies that raise questions about decreased decisional ability in some subjects. Questions from potential participants and family members should be encouraged, and handouts of frequently asked questions and answers regarding specific human subject protections may be prepared. Communication between members of the research team, participants, and their families is key to successful research participation.

Individuals who are decisionally impaired may need more time to consider the information they are given about a research protocol. Information should be provided incrementally to facilitate understanding. Planning built-in waiting periods within the consent process may be useful to allow potential participants time to consult with family members about whether or not to participate.

Finally, for all studies that raise questions about some of the subjects' ability to participate in the informed consent process, the Principal Investigator should plan and deliver ongoing educational efforts with subjects during the lifetime of the study to enhance research participants' understanding and appreciation of their role in the research. Because informed consent is an ongoing process throughout the course of a protocol, assessing and enhancing comprehension at each stage is essential. Single sheet summaries of important information about key elements of a study may be useful when provided on a regular basis.

When submitting new research applications for studies which will involve subjects who may lack decisional ability or may be reasonably expected to develop decisional impairment during the course of the study, Investigators must address the following three questions in the eBridge Study SmartForm application and describe other proposed safeguards for this vulnerable population.

1. **Can the research objectives be satisfied without enrolling decisionally impaired subjects?** The investigator must provide rationale for why the study includes individuals who have decreased decisional ability or may develop decreased decisional abilities, and explain why the study could not be done without enrolling decisionally impaired subjects.

2. **How does the investigator propose to assess the decisional ability of subjects prior to study enrollment?** An assessment of the subject's ability to consent should take place before each subject is enrolled in the study. The investigator should include a detailed description of the screening process and instruments to be employed. If the investigator believes that it is not necessary to assess decisional competence prior to enrollment into the study the investigator should provide a clear rationale for not performing an assessment.
Assessments of potential subjects:
The investigator should describe how the assessment will be performed and identify the assessors. The ideal person to assess decisional ability varies according to the nature of the study. Factors to be considered in a description of the assessment procedures include:

- The potential subject's underlying condition(s);
- The complexity of the study protocol;
- The level of risks inherent to the study;
- The voluntary or coerced quality of the potential subject's consent, in light of the subject's relationship with the physicians conducting the study or the acute nature of the disease.

Documentation of the assessment(s) and results must be noted in the research record for all enrolled subjects.

Possible assessment procedures might include any one or a combination of the following activities:

- use of independent "consent monitors" to witness or supervise the informed consent process;
- assessment of decisional ability by an identified subset of qualified, trained study staff. The qualifications and training of those named as "qualified assessors" should be discussed in detail;
- assessment of decisional ability by an independent assessor.
- assessment undertaken by a physician or registered clinical psychologist whose professional training and credentials are suitable given the nature of the subject's condition and the nature of study; and/or
- a brief quiz following a full discussion of the study. The quiz questions should test an essential understanding of:
  - voluntary participation in research;
  - the nature of the study procedure, intervention, etc.;
  - reasons for doing the procedure;
  - consequences of not doing the procedure;
  - risks of involvement in the study; and
  - alternative options or treatments.

Participants who fail to provide accurate answers to the quiz items may benefit from further discussion, review of the consent form, and more education about the study, followed by a second administration of the quiz. Accurate responses to the second administration imply ability to provide informed consent. Incorrect answers to the second administration would support the assumption of impaired decisional ability for the study in question; the research team should not try to consent the subject more than two times in the same day.

3. **How does the investigator propose to monitor the decisional ability of subjects over the course of the study?** If there is a likelihood that a subject's decisional ability may change or decline during the course of a study, then the investigator should describe procedures for monitoring the subjects over time to evaluate decisional ability, detect loss of ability, and remove subjects with decisional impairment from the study.
The ideal person to monitor decisional ability varies according to the nature of the study. Overall, the subject must be seen and assessed with sufficient frequency to detect changes in the subject’s health and decisional abilities. The investigator should describe exactly how often the assessments will be repeated, and the location at which monitoring will be done (hospital, office, or home).

Possible monitoring processes include:

a. Monitoring of decisional ability by identified qualified study staff. The qualifications and training of those named as “qualified assessors” should be described in detail;

b. Monitoring by a physician or registered clinical psychologist whose professional training and credentials are suitable given the nature of the subject’s condition and the nature of the study.

c. Allowing decisional subjects to complete a formal “advance directive” on enrollment into the study, detailing their reasons for wanting to participate in the study and the circumstances under which they would likely want to withdraw from the study. Documenting these thoughts at the beginning of the study might help inform and guide their LAR, should the subject experience decreased decisional ability during the course of the study.

d. Monitoring of decisional ability by someone independent from the research team, such as a primary care physician or attending physician. For some protocols, a “home monitor” might be identified who can evaluate the subject on a more frequent basis. The “home monitor” should be a reliable adult relative or friend who lives in close proximity to the subject and who is capable of reporting changes in the subject’s status to the investigators with objectivity.

Obtaining informed consent from Legally Authorized Representatives (LARs)

When the investigator has documented that the subject lacks decisional ability, or has lost decisional ability, the subject may not be enrolled into the study or allowed to continue the study unless the appropriate LAR has provided documented informed consent and unless the subject has provided his/her assent (when possible). In the situation where the LAR provides informed consent but the subject does not assent (assuming the subject has any capacity to assent), the subject may not be enrolled or continued in the study. The LAR should make the decision about study participation based on his/her understanding of the subject’s wishes and values, not those of the LAR. When discussing a study or consent with an LAR, Investigators should allow them generous amounts of time to consider information about the research study and make a decision. It is often better to provide information in increments (over a period of days) to facilitate understanding.

Good and frequent communication among members of the research team, subjects, their family members and caretakers, and their LARs is a key marker for demonstrating “respect for persons” with this vulnerable population. Investigators should consider various methods to ensure clear communication among all parties, include encouraging questions and preparing handouts of frequently asked questions (FAQ).
IRB Review
MCW/FH IRB imposes additional protections when reviewing research involving individuals who have or may develop decreased decisional abilities. Federal regulations outline the relevant criteria for deciding whether to approve a study including: (a) the overall level of study risk; (b) the prospect of direct benefit to individual subjects; and (c) the likelihood that the study will yield “generalizable knowledge about the subjects’ disorder or condition which is of VITAL importance for the understanding or amelioration of the disorder/condition.”

- For studies which may represent more than “minimal risk” to subjects, the IRB is reluctant to approve enrollment of individuals who lack decisional ability; and thus cannot give informed consent unless: (a) there is meaningful prospect of direct benefit to the individual subject; and/or (b) the potential subject has completed an advance directive about participation in a specific study which may guide the LAR.
- For studies which represent a “minor increase over minimal risk” (e.g., MRI with sedation, indwelling catheters for short duration), the IRB may recommend additional safeguard protections on a study-by-study-basis.

The IRB reviewing the proposed study will be guided by this procedure and the IRB procedure: Legally Authorized Representatives (LARs): Who Can Consent to Research on Behalf of an Adult Subject with Decreased Decisional Ability? to ensure proper safeguards and protections are implemented.

When issuing documentation of approval for a study of subjects likely to manifest or develop decreased decisional ability, the approval letter will indicate that the investigator has approval to enroll subjects with decisional impairment, contingent upon listed extra protections.

REFERENCES:
Legally Authorized Representatives (LARs): Who Can Consent to Research on Behalf of an Adult Subject with Decreased Decisional Ability

ATTACHMENTS:
N/A

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