



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: 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). If 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 project 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 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: 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., intellectual disability), 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 project team and/or associated with the conduct of the project 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 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 project. The independent assessor should not be included as an author on any presentation or publication reporting on the project.

POLICY:

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 project, 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 project.

When the subject lacks decisional ability, the Investigator must obtain informed consent from a legally authorized representative, and 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 project, but their condition may change or deteriorate over the course of the project. When a subject in an ongoing project loses his/her decisional ability (transiently or irreversibly), the subject's participation in the project 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 project, but are still capable of consent:

- discuss whether the prospective subject would want to continue project 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 *IRB SOP: 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 projects, informed consent should not be elicited and documented on the same day that the subject is first presented with information about the project. This principle is particularly important for projects 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 participation.

Finally, for all projects that raise questions about some of the subjects' ability to participate in the consent process, the Principal Investigator should plan and deliver ongoing educational efforts with subjects during the lifetime of the project 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 project may be useful when provided on a regular basis.

PROCEDURES:

When submitting new research applications for projects which will involve subjects who may lack decisional ability or may be reasonably expected to develop decisional impairment during the project, Investigators must address the following three questions in the eBridge SmartForm 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 project includes individuals who have decreased decisional ability or may develop decreased decisional abilities, and explain why the project could not be done without enrolling decisionally impaired subjects.

2. How does the investigator propose to assess the decisional ability of subjects prior to project enrollment? An assessment of the subject's ability to consent should take place before each subject is enrolled in the project. 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 project 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 project. Factors to be considered in a description of the assessment procedures include:

- a. The potential subject's underlying condition(s);
- b. The complexity of the project;

- c. The level of risks inherent to the project;
- d. The voluntary or coerced quality of the potential subject's consent, considering the subject's relationship with the physicians conducting the project 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 anyone or a combination of the following activities:

- a. use of independent "consent monitors" to witness or supervise the
- b. informed consent process;
- c. assessment of decisional ability by an identified subset of qualified,
- d. trained staff. The qualifications and training of those named as
- e. "qualified assessors" should be discussed in detail;
- f. assessment of decisional ability by an independent assessor.
- g. 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 project; and/or
- h. a brief quiz following a full discussion of the project.

The quiz questions should test an essential understanding of:

- a. voluntary participation in research;
- b. the nature of the project procedures, intervention, etc.;
- c. reasons for doing the procedure;
- d. consequences of not doing the procedure;
- e. risks of involvement in the project; and
- f. 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 project, 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 project 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 project? If there is a likelihood that a subject's decisional ability may change or decline during a project, 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 project.

The ideal person to monitor decisional ability varies according to the nature of the project. 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 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 project.

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

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 project or allowed to continue the project 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 project. The LAR should make the decision about project participation based on his/her understanding of the subject's wishes and values, not those of the LAR. When discussing a project or consent with an LAR, Investigators should allow them generous amounts of time to consider information about the research project 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 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 project including: (a) the overall level of risk; (b) the prospect of direct benefit to individual subjects; and (c) the likelihood that the project 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 projects 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 project which may guide the LAR.

- For projects 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 project-by project-basis.

REFERENCES:

45 CFR 46.101(i)
45 CFR 46.102 (c)
45 CFR 46.116(c)(d)
21 CFR 50.3 (1)

SUPPORTING DOCUMENTS:

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

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