4.6 IRB Review of Research Involving Subjects with Impaired Decision-Making Capacity

1.0 Purpose

The purpose of this policy is to describe the Organization's requirements for IRB review of research involving subjects who have impaired decision-making capacity.

2.0 Policy

It is the policy of the Organization that research involving subjects who have impaired decision-making capacity must include appropriate additional protections in accordance with the ethical principles described in the Belmont Report, and the requirements of 45 CFR 46.111(b) and 21 CFR 56.111(b), as applicable.

3.0 Definitions

- 3.1. Decisionally impaired person, in the context of human subject research, means an adult with diminished capacity for judgment and reasoning such that he/she is unable to make an informed, voluntary decision to participate in research. The impairment which leads to this diminished capacity may be a temporary acute condition, may fluctuate, or may be a more long-term or permanent condition. It may be the result of any psychiatric disorder, an organic impairment, a developmental disorder, or severe acute illnesses associated with cognitive impairment.
  Note: Capacity, defined as an individual's ability to make an informed decision should not be confused with competence. Competence is a legal state, not a medical one. Competence refers to the degree of mental soundness necessary to make decisions about a specific issue or to carry out a specific act. All adults are presumed to be competent unless adjudicated otherwise by a court. Incompetence is defined by one's functional deficits, which are judged to be sufficiently great that the person cannot meet the demands of a specific decision-making situation, weighed in light of its potential consequences. Only a court can make a determination of incompetence.
- 3.2. Legally Authorized Representative (LAR) is defined as "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. If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research" (45 CFR 46.102(i)). "Legally authorized representative" in the context of research is, however, not defined in the Nebraska revised statutes. OHRP Guidance notes that "In these states {that have no law specifically addressing the issue of consent in the research context}, law that addresses who is authorized to give consent on behalf of another person to specific medical procedures or generally to medical treatment may be relevant if the research involves those medical procedures or medical treatment. When the laws of the jurisdiction in which the research is being conducted provide a reasonable basis for authorizing an individual to consent on behalf of a prospective subject to their participation in the research procedure(s), OHRP would consider such an individual to be an LAR as defined by HHS regulations at 45 CFR 46.102(c)."
  - 3.2.1. Under Nebraska law, the following persons may serve as a Legally Authorized Representative
    - 3.2.1.1. Parents and guardians having legal custody of the decisionally impaired person.
    - 3.2.1.2. The court-appointed legal guardian of the decisionally impaired person in accordance with Neb. Rev. Stat. 30-2627.
    - 3.2.1.3. The individual authorized to consent on behalf of a decisionally impaired person pursuant to a legally effective Health Care Power of Attorney (POA-HC).
  - 3.2.2. In addition, Institutionally Authorized Surrogate (IAS), as defined per Section 3.3 below, may serve as a LAR for the purpose of this policy, except the IAS may not provide consent (permission) for category 3 research, as discussed in section 7.3 below.
- 3.3. Institutionally Authorized Surrogate (IAS) is defined as a person authorized by the Organization to provide consent for medical procedures and tests for a patient who lacks capacity, and for whom there is not an LAR under Nebraska law as described above. Persons who may act as IAS, and the priority order of such persons, are described in Nebraska Medicine policy MS14 (Consents and Permits)
- 3.4. Adult assent is defined as the affirmative agreement of a decisionally impaired person to participate in research.
- 3.5. Dissent is defined as an objection to participation. In general, dissent is considered

meaningful if it is unequivocal or sustained after an effort to relieve concerns and/or distress (Black B, et al; Am J Geriatr Psychiatry 18(1), 77-85, 2010)

4.0 Assessment of Capacity to Consent

- 4.1. The determination that a prospective subject is decisionally-impaired and, therefore, lacks the capacity to provide legally effective informed consent may have been: a) adjudicated by the Court, or b) determined by an investigator, who, by their professional training, licensure, or experience, is qualified to determine capacity, or c) determined by an independent assessor.
- 4.2. The method utilized to determine capacity may vary depending on the characteristics of the research protocol (including the risks and the risk-benefit relationship) and of the subject population. In general, with increasing risks, less favorable risk-benefit relationship, expected higher proportion of cognitively impaired subjects, or expected greater depth of impairment, the assessment of capacity should utilize more formal tools. Standard tools include, but are not limited to:
  - 4.2.1. Clinical interviews
  - 4.2.2. Mini-Mental Status Exam (MMSE)
  - 4.2.3. “Assessment of Capacity to Consent to Participate in Research” instrument available on the IRB website.
  - 4.2.4. MacArthur Competency Assessment Tool for Clinical Research (MacCat-CR),
- 4.3. For research studies involving higher risks, less favorable risk-benefit relationship, expected higher proportion of cognitively impaired subjects, or expected greater depth of impairment, the investigator should consider the use of an independent, experienced assessor and/or an independent monitor of the consent/assent process.
- 4.4. Researchers should reassess capacity for individuals who exhibit fluctuating capacity levels, or if the research involves a population where it would be reasonably expected that capacity would be regained for at least some of the subjects.

5.0 Appointment and Authority of the LAR

- 5.1. If an individual lacks the capacity to consent, they can only be enrolled in research only if an LAR provides consent on their behalf.
- 5.2. If a prospective subject does not have an LAR as defined in Section 3.2 above, an IAS should be appointed.
- 5.3. The prospective subject’s capacity to choose an IAS should be assessed and, when possible, the subject’s choice should be honored.
- 5.4. Availability, willingness and capacity to serve as a responsible surrogate decision-maker should be considered in the appointment of an IAS.
- 5.5. The LAR should normally use “substituted judgment” where possible as opposed to “best interests”. It is important for the LAR to consider what would be the subject’s position given a choice whether or not to participate in the research when they were not cognitively impaired.

6.0 Assent and Dissent

- 6.1. The investigator must make adequate provisions for soliciting the assent of the decisionally impaired persons, when in the judgment of the investigator and the IRB they are capable of providing assent.
- 6.2. If the investigator and the IRB determine that the capability of some or all of the potential subjects of the research is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the potential subjects and is available only in the context of the research, the assent of the decisionally impaired persons is not a necessary condition for proceeding with the research.
- 6.3. If a decisionally impaired person exhibits unequivocal or sustained dissent to initially participate in research, that dissent must be honored as long as the research does not hold out the prospect of direct subject benefit that is only available in the context of the research. If the research holds the prospect of direct subject benefit, approval to override the decisionally impaired person’s dissent and enroll the individual in the research must be obtained from the IRB Executive Chair. The full IRB will be notified of the IRB Executive Chair’s decision, and the board has the authority to accept the IRB Executive Chair’s decision, require additional actions, or require withdrawal of the subject.
- 6.4. If a decisionally impaired person exhibits unequivocal or sustained dissent while participating in research, that dissent must be honored as long as the research does not hold out the prospect of direct subject benefit that is only available in the context of the research. If the research holds the prospect of direct subject benefit, approval to override the decisionally impaired person’s dissent and continue the subject’s participation in the research must be obtained from the IRB Executive Chair. The full IRB will be notified of the IRB Executive Chair’s decision, and the board has the authority to accept the IRB Executive Chair’s decision, require additional actions, or require withdrawal of the subject

7.0 Acceptable Research Involving Decisionally Impaired Subjects

- 7.1. Category 1 - Minimal risk:
  A decisionally impaired subject may participate in research involving minimal risk with no direct subject benefit if an LAR or IAS provides consent, and the decisionally impaired person provides assent (as described in section 6 above).
- 7.2. Category 2 – Greater than minimal risk with the prospect of direct benefit:
  A decisionally impaired subject may participate in research involving greater than minimal risk and a prospect of direct benefit if:
  - 7.2.1. The risk-benefit relationship is favorable, and
  - 7.2.2. The risk-benefit relationship is at least as favorable as available alternative therapies, and
  - 7.2.3. An LAR or IAS provides consent, and the decisionally impaired person provides assent (as described in section 6 above).
- 7.3. Category 3 - Greater than minimal risk with no prospect of direct benefit:
  A decisionally impaired subject may participate in research involving greater than minimal risk without prospect of direct benefit only if:
  - 7.3.1. The research represents only a minor increase over minimal risk, and
  - 7.3.2. The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual medical, dental, psychological, social, or educational situations; and
  - 7.3.3. The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
  - 7.3.4. An LAR provides consent, and the decisionally impaired person provides assent (as described in section 6 above).
    Note: an IAS is not authorized to provide consent for category 3 research
- 7.4. Cognitively impaired persons may not be enrolled into research which does not fall into one of the above 3 categories.
- 7.5. Cognitively impaired persons who are under a court mandated therapy for a psychiatric disorder are not eligible to participate in research.

8.0 Additional Protections

In consideration of the characteristics of the subject population, the nature of the research and the risk level, the IRB will determine what additional protections are necessary. Additional protections for vulnerable subject populations which include individuals who are decisionally impaired are described in HRPP policy 4.1 (Additional Protections for Vulnerable Populations).

9.0 IRB Review

- 9.1. Applications which require review by the full IRB will be processed and reviewed in accordance with HRPP policy 2.2 (Full IRB Review). In consideration of the nature of the protocol, one or more IRB members who are knowledgeable about and experienced in working with decisionally impaired persons will be involved in the review. In some circumstances, a consultant will be appointed to assist the IRB in their review.
- 9.2. Applications that are eligible for review by the expedited method will be processed and reviewed in accordance with HRPP policy 2.3 (Expedited Review). In consideration of the nature of the protocol, one or more IRB members who are knowledgeable about and experienced in working with decisionally impaired persons will be involved in the review
- 9.3. The IRB will determine whether the research is allowable as per section 7.0 above, whether there are adequate additional protections for vulnerable populations, whether assent and dissent will be managed in accordance with section 6, whether capacity is being assessed adequately, and whether there are adequate plans for re-consent or withdrawal should a subject regain capacity.

10.0 Disclosure and Consent for Continuing Participation

If a person with diminished capacity regains capacity during the conduct of the research, he/she must be fully informed about the research and the circumstances of his/her enrollment. His/her consent to continue in the research protocol must be obtained in accordance with HRPP policy 5.1 (Obtaining Informed Consent from Research Subjects).

11.0 Disclosure After the Research has Been Completed

If a person with diminished capacity regains capacity following completion of the conduct of the research, he/she must be fully informed about the research and the circumstances of his/her enrollment.

12.0 Consent Forms/Adult Information Sheet

- 12.1. Informed consent (permission) of the LAR or IAS will be documented in accordance with HRPP Policy 5.1 (Obtaining Informed Consent from Research Subjects)
- 12.2. As appropriate, subjects with impaired decisional making capacity will be provided with an Adult Information Sheet. The Adult Information Sheet should be written in simple language aimed at the appropriate cognitive level of the decisionally impaired subjects to be enrolled in the study. The adult information sheet should contain the elements of assent that are found in the Information Sheet Template.

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