

Research Integrity Office

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Human Subjects Research
with Decisionally Impaired Adults

Introduction

Human subjects research involving persons who have impaired decision-making capacity is an important endeavor for advancing the treatment of such persons. This document provides guidance on how human subjects research at OHSU should be conducted when it involves decisionally impaired (DI) adults.

This Help Sheet is a supplement to:

- POLICY HRP-021: Legally Authorized Representatives, Children, and Guardians
- INVESTIGATOR GUIDANCE HRP-802: Informed Consent
- WORKSHEET HRP-414: Adults Lacking Capacity

The IRB uses “**WORKSHEET HRP-414: Adults Lacking Capacity**” when reviewing research involving DI adults. You can help your review go smoothly by ensuring that all of the items on this worksheet that apply to your study are addressed in your protocol or other study documents.

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1. Defining Risks and Benefits

To approve any research study, the IRB must find that the risks to subjects are minimized and that the anticipated risk/benefit ratio of the study is appropriate. Consider the impact of potential subjects’ decisional impairment on the risks and benefits of your study. Procedures that generally pose minimal risk may pose greater risk to subjects with decisional impairment, and vice versa. Think about whether additional safety or monitoring procedures are needed to minimize risk for this population. If subjects are not expected to benefit directly from participating in the research, the scientific rationale for including decisionally impaired subjects must be particularly strong.

2. Defining and Assessing Capacity

Your protocol must describe an appropriate plan for assessing the decision-making capacity of potential subjects. This may include assessment of capacity at various points in the recruitment and consent process, depending on the circumstances and the subject population. Consider whether subjects are likely to have complete, progressive, fluctuating, or temporary decisional impairment, and how this will affect your ongoing assessment of their capacity to consent.

The IRB does not prescribe standardized methods or measures for PIs to use when assessing a prospective subject's capacity. However, a person with capacity to consent should generally be able to understand the following concepts:

- Nature of the research and the information relevant to his/her participation;
- Consequences of participation for the subject's own situation, especially concerning the subject's health condition;
- The difference between research and clinical care (avoiding therapeutic misconception);
- Available alternatives to participation and their consequences;
- Potential risks involved in the study;
- Procedures to follow if he/she experience discomfort or wishes to withdraw; and
- The voluntary nature of participation.

3. Obtaining Informed Consent and Assent

An adult subject who lacks decision-making capacity may participate in research only if consent is obtained by a Legally Authorized Representative (LAR) acting on the subject's behalf. An individual acting as an LAR must be able to understand the concepts listed in section 2 in order to provide consent on behalf of the subject. Whenever possible, assent of the subject must also be obtained.

The protocol must describe an appropriate plan for obtaining the informed consent of an LAR and, if applicable, assent of the subject.

a. Designating an LAR

As stated in POLICY HRP-021, the following individuals may serve as an LAR for an adult subject who lacks capacity to consent, in order of priority:

- 1) Health care representative who is legally authorized by a valid advance directive or health care power of attorney
- 2) Court-appointed guardian
- 3) If the above two do not exist or cannot be located with reasonable effort, another surrogate who knows and can represent the previously expressed wishes of the potential subject, in the following order of preference:
 - a) Spouse or registered domestic partner
 - b) Adult child
 - c) Either parent
 - d) Adult sibling
 - e) Adult designated by others on this list, if no one on the list objects
 - f) Other adult relative or friend who has an established relationship with the potential subject

When an LAR is making a decision to enroll a DI adult into a research study, the LAR's decision must reflect the subject's prior values insofar as they are known or can be determined. In meeting this standard, the following may be considered: prospective permission (e.g. an advance directive that speaks to a specific study or category of research); statements made by the subject when he/she had no decisional impairment about categories of research, risks related to research, or research participation in general; previous research participation by the subject; and testimony from others who are well acquainted with the subject and likely to be familiar with his/her values including relatives, friends, or health care providers.

The greater the risks posed by the research, the more stringent will be the requirement for evidence of the prospective subject's desire to participate in order to entitle the LAR to permit enrollment. If the subject's values are not known, the LAR should act in the subject's best interest given the anticipated risks and benefits of participation in the research.

Likewise, what is considered "reasonable effort" to reach the highest-priority LAR available will vary depending on the nature of the study. Generally, greater effort must be made when the risk of the study is higher and/or the anticipated benefit to the subject is lower. However, other factors may be relevant, such as a limited timeframe within which the subject must begin study-related treatment or the importance of the knowledge to be gained about the subject's disease or condition. Higher risk protocols should specifically discuss procedures for attempting to contact potential LARs in order of priority.

If two or more available LARs disagree regarding a potential subject's enrollment in the study, the subject should not be enrolled.

b. Assent

Unless the subject has severe decisional impairment (unconscious, delirious) prior to participation in research, an investigator shall obtain the subject's assent after informing the subject of the following, in a manner appropriate to the subject's capacity for understanding:

- The fact that he/she is being asked to participate in research;
- That he/she has been determined to lack capacity to self-consent to research participation;
- The name of the LAR who has been identified, that he or she has granted permission for the subject's participation in the research, and the extent to which the LAR will be involved in the subject's research participation;
- Information about the purpose, design, procedures, risks and benefits, and potential personal impacts of the research study; and
- That the subject may choose freely to undergo these procedures or may withdraw from participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

A subject who expresses resistance or dissent to participation or to the use of LAR consent should not be enrolled in the study.

c. Ongoing Consent

In cases of temporary, fluctuating or progressive decisional impairment, a subject's capacity to consent may change throughout the study. If a subject regains capacity to consent, the subject shall have the opportunity to provide informed consent for his or her own continued participation. Likewise, when a subject loses capacity, consent for the subject's continued participation shall be obtained from an LAR. When it is anticipated that subjects may lose capacity to consent during the course of the research, the IRB recommends involving an individual of the subject's choice at the beginning of the study who may later serve as an LAR.

An LAR does not necessarily need to be the same person throughout the study, as long as the LAR meets the criteria described above.

Additional Resources

National Institutes of Health, "[Research Involving Individuals with Questionable Capacity to Consent: Points to Consider](#)" (November 2009)

National Bioethics Advisory Commission (NBAC), "[Research Involving Persons with Mental Disorders That May Affect Decision-Making Capacity](#)" (December 1998)

OHRP Guidance: [Informed Consent FAQs](#)