



THE USE OF THE LEGALLY AUTHORIZED REPRESENTATIVE IN RESEARCH INVOLVING A VULNERABLE POPULATION OF ADULT SUBJECTS

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Federal regulations that govern research involving human subjects define a legally authorized representative (LAR) 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 [45 CFR 46.102(c) and 21 CFR 50.3(l)].

North Carolina law permits consent for therapeutic clinical research to be provided by the same individuals as those who are entitled to authorize consent to medical treatment generally.

In accordance with DUHS policy regarding informed consent for treatment, the order of authority to provide consent on behalf of another adult for participation in clinical research presenting the prospect of therapeutic benefit to the subject is as follows:

- Court-approved guardian
- Health care agent
- Spouse
- Adult son and/or daughter
- Parent
- Adult brother and/or sister
- Uncle and/or aunt
- Other adult kin

Federal regulations governing research involving certain vulnerable populations contain more specific requirements:

For research involving pregnant women and/or fetuses, see 45 CFR 46.204.

For research involving neonates, see 45 CFR 46.205.

For research involving children, the parent or the child's legal guardian is authorized to give permission for the child's participation in research. The child's guardian is defined as an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care [45 CFR 46.402(e)]. Under North Carolina law, a guardian of a child must be appointed by a court under Article 6 of Chapter 35A of the North Carolina General Statutes.

The IRB, when initially approving the use of a legally authorized representative for adult participants in a particular research protocol, will do so during a convened meeting. Subsequent approval at the time of Continuing Review may occur using the expedited procedure under Category 9 of "Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure".

The Use of the LAR in the Setting of Non-Therapeutic Research



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As determined by University Counsel, the statement below must be added to a consent form that will be signed by a legally authorized representative on behalf of an adult research participant, but *only in the setting of non-therapeutic research*, where there is no prospect of direct therapeutic benefit to the study participant:

"I am the representative of the subject and am acting on behalf of the subject. I am not aware of any factor that might create a conflicting interest for me in this role (for example, something that might bring me personal benefit). I consent to the subject's participation in this study."

The IRB, when approving the use of a legally authorized representative in the setting of non-therapeutic research, will require that this statement be added to the consent form.

IRB Considerations Concerning Use of the LAR

The IRB may consider the following points as the members evaluate research for which the investigator requests that the subject's legally authorized representative be permitted to act on behalf of the subject:

- Is the information or knowledge to be gained by way of the research project important? Can it be obtained in a way other than by including such vulnerable subjects?
- Is the inclusion of the vulnerable population necessary to answer the research question?
- Does the research pertain specifically to the vulnerable population?
- Has the research been preceded by adequate preclinical and clinical studies?
- Is the risk of study participation judged to be minimal or more than minimal?
- Does research participation offer the prospect of direct therapeutic benefit to the subject?
- Does the research offer the prospect of other direct benefit to an individual subject?
- Are the procedures appropriate for determining whether the subject has impaired decision-making such that the subject cannot give legally effective informed consent?
- Should the subject's decision-making capacity be assessed by an independent physician?
- Should the consent process be monitored?
- Should a research subject advocate be involved in the consent process, initially or throughout the course of the study?
- Is assent of the subject required if the subject is thought to be capable of assenting?

Investigator Considerations

Assessing Decision-Making Capacity

A potential research subject is generally regarded as having decision-making capacity to act on his/her own behalf if s/he demonstrates an understanding of the difference between treatment



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and research, demonstrates an understanding of the risks and benefits of study participation and the alternatives to study participation, and can make a decision.

In order to determine the decision-making capacity of the potential subject, a qualified health care professional must perform a formal evaluation, such as a psychiatric evaluation or a medical assessment, which considers what level of understanding is necessary for the specific research. Commonly used measures to assess decision-making capacity, such as the Mini Mental Status Exam, may be helpful, but should not be the sole measure of decision-making capacity.

The investigator must describe how decision-making capacity will be assessed and by whom, and how that person is related to the potential subject and/or the study.

Who May Assent

In some cases, a subject may be capable of assenting to participate in research by signing the informed consent form even though it has been determined that a LAR should also sign. In determining whether the subject may be capable of assenting, the IRB should take into account the mental capacity and the psychological state of the subjects involved. This judgment may be made for all subjects involved in the research under a particular protocol, or for each subject, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the subjects is so limited that they cannot reasonably give their assent, the IRB may find that the assent of the subject is not a necessary condition for proceeding with the research.