IRB Review of Research Involving Potential Subjects Lacking Consent Capacity

Impairment of an adult's capacity to consent to research participation may be due various factors such as dementia (most commonly Alzheimer's disease), traumatic brain injury, developmental disorders, intellectual disabilities, or serious mental illness. Progress in early detection, diagnosis and treatment of these disorders requires inclusion of such participants in research. Additionally, individuals who lack consent capacity may be eligible for studies of conditions unrelated to their cognitive impairment that have prospect of direct benefit. Among the criteria for IRB approval of research, the HHS regulations notes the IRB must determine that "When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects." (See 45 CFR 346.111b.) The regulations do not include a separate subpart describing protections for those with impaired decision making as they do for pregnant women/human fetuses/neonates, prisoners, and children. However, the Secretary's Advisory Committee on Human Research Protections (SACHRP) provided Recommendations Regarding Research Involving Individuals with Impaired Decision-making to the HHS Secretary in 2009.

IRB review of protocols that propose to enroll participants who lack consent capacity

- The protocol should explicitly justify the rationale for enrollment of those who lack consent capacity and, as applicable, what safeguards will be in place. If subjects who originally have consent capacity may lose capacity, the protocol should describe conditions under which they may continue to participate in the study.
- Consider whether inclusion of individuals who lack consent capacity is ethically appropriate and scientifically necessary (e.g., the research aims to improve understanding, detection, diagnosis, or treatment of the disorders that cause the incapacity). Alternatively, can the scientific question be answered by studying individuals who retain consent capacity?
- If potential subjects may lack consent capacity, the IRB should consider if the method to assess capacity as described in the protocol, as well as plans for who will provide this assessment, are adequate.
- The level of consent capacity that is needed will vary depending on the complexity of the study and risk level.
- When consent will be obtained from the subjects' legally authorized representative (LAR), the protocol should include information about the process for obtaining consent/reconsent from the LAR.
- Per NIH Policy 3014-403, *Research Involving Adults Who Lack Decision-making Capacity to Consent to Research Participation*, the NIH IRB may only approve research that permits the participation of subjects without consent capacity if it determines and documents that the research meets one of the following risk/benefit categories:
  - The research is minimal risk (Category A)
  - The research is greater than minimal risk, and offers a prospect of direct benefit to the participant (Category B)
  - The research is no more than a minor increase over minimal risk with no prospect of direct benefit, and does not adversely affect the rights, safety, or welfare of the participants (Category C) or
  - Research does not meet the above conditions but has undergone additional institutional review and approval by the NIH IO (Category D)
- The IRB should carefully review the consent process as described in the protocol (e.g., How will consent be obtained from the LAR? How will the validity of the LAR be determined? Are safeguards proposed in the protocol regarding the consent process adequate or are additional safeguards needed?)

Possible safeguards are based on level of risk proposed by the research

The IRB should determine if appropriate safeguards are in place.

- If the potential subject lacks the capacity to consent to research participation, consent must be obtained from their LAR, and hierarchy for determining who may serve as the LAR at an NIH site is detailed in NIH Policy 3014-403, *Research Involving Adults Who Lack Decision-making Capacity to Consent to Research Participation*.
- For studies that pose greater than minimal risk, consider whether consent capacity assessments should be conducted by a qualified professional who is independent of the study team.
- Consider if consent monitoring or assent by the potential subject (verbal or written) should be required.

Category	Risk/Benefit level	Level of Review Required	Hierarchy for determining the LAR at an NIH site (For research conducted at non-NIH sites, this may vary due to state law or institutional policy)
Category A	Minimal risk	IRB (expedited or full board)	1. Court-appointed guardian of the person, who is authorized to consent to the research [1] 2. The individual(s) appointed in the patient's Durable Power of Attorney (DPA) for health care 3. If the prospective subject does not have a court-appointed guardian or DPA for health care, and they are capable of understanding the DPA process, even if they lack capacity to consent to research, the prospective subject may execute a DPA for health care 4. If no court-appointed guardian or DPA for health care exists, and the prospective subject is unable to execute a DPA for health care, then the next of kin hierarchy listed below may be used to identify the LAR in the following descending order: a. Spouse or domestic partner b. Adult child c. Parent d. Adult sibling, or e. Other relative
Category B	GTMR but offers prospect of direct benefit (DB)	Full Board IRB review	Same as above for Category A
Category C	No more than a minor increase over minimal risk with no prospect of DB and does not adversely affect the rights, safety, or welfare of participants	Full Board IRB review	Same as above for Category A
Category D	Research that does not fall into one of the above categories	Requires institutional review and approval by the NIH Institutional Official followed by full Board IRB review	• There must be a court-appointed guardian or DPA for health care who may provide consent on behalf of the participant. • The next of kin hierarchy (as listed above) may **not** be used to identify an LAR.

[1] A court-appointed guardian may only consent for a subject without capacity to participate in research if the guardian has authority to do so under the laws of the state that issued the guardianship order and the terms of the guardianship order.