

Informed Consent and Assessment of Capacity to Consent to Research Policy

Scope

Mayo Clinic Human Research Protection Program

Relying Organizations for which the Mayo Clinic IRB is the IRB of Record

Purpose

This policy provides guidance to the Mayo Clinic Office for Human Research Protection Institutional Review Board (IRB) and to investigators when considering the inclusion of individuals with decisional impairments in research, or when drawing research participants from a population likely to have impaired consent capacity

Background

The ethical principle of equitable subject selection prohibits selective exclusion of individuals with diminished autonomy from research participation, though additional protections for these individuals are required. Some individuals with diminished autonomy may still be capable of providing consent to enroll into a research study. Investigators must seek ways to enable the participation of these individuals in an ethically acceptable manner that promotes their autonomy while complying with regulatory requirements and guidance as well as institutional policies.

Consent capacity can be affected by such conditions as mental disorders, neurological disorders, metabolic impairments, or head trauma, or by psychoactive medications and substance abuse. In some situations, these conditions may produce substantial impairment of capacity, while in other situations they may not affect an individual's understanding of required informed consent elements. In research involving participants with such conditions, investigators and the IRB must consider and determine whether a prospective subject's diminished decision-making capacity affects capability to provide informed consent.

An individual's capacity to provide informed consent can also be affected by other types of vulnerability such as poverty or deficits in education, or transient situations where an individual is in emotional or physical crisis, such as having just received a diagnosis of serious illness or receiving care for an injury in the Emergency Department.

Policy

Investigator Responsibilities

For studies planning to enroll participants who may have impaired consent capacity, or when drawing research participants from a population likely to have impaired consent capacity, the Investigator:

- Will consider, and describe within the protocol or IRB application, justification for inclusion of individuals who lack consent capacity and address the inclusion in terms of ethical appropriateness and scientific necessity for the proposed study.
- Will ensure that the methodology which will be used for the consenting process is described within the protocol or IRB application. Methods will be consistent with the Common Rule and the ethical principles outlined in the Belmont Report. The method(s) must be commensurate with the degree of understanding exhibited by

the participant, the level of risk to the participant, the complexity of the research, and the anticipated duration of the participant's involvement. Investigators will consider additional safeguards to ensure the voluntariness of study participation.

- *Will describe assessment methods and instruments within the protocol or IRB application that will be used in evaluating the capacity of a potential participant to provide initial and continued consent.

***Refer to ["Guidance for Investigators and the IRB: Informed Consent and Assessment of Capacity to Consent to Research"](#), item #1 under the heading "Investigator responsibilities for studies planning to enroll participants with impaired consent capacity".**

- Will consider, and document within the protocol or IRB application, methods for re-evaluating participant's capacity to consent over the course of the study, including methods for consenting at the time participant regains capacity, as applicable. See section titled "Fluctuating Consent" within this policy.
- As applicable, will consider, and document within the protocol or IRB application, the involvement of a legally authorized representative (LAR). When a LAR is acting on behalf of the potential participant, investigators must consider the most appropriate methods to present information about the study to both the LAR and the participant, including its risks and anticipated benefits. State or local law may also be relevant to the involvement of LARs and the conduct of research involving individuals with impaired consent capacity. Refer to section in this policy titled "Surrogate Consent".
- When applicable, will consider and describe within the protocol or IRB application, procedures for obtaining the assent of adult participants who cannot consent. Refer to section in this policy titled "Surrogate Consent".
- Will be responsible for training the study team, as needed, to administer consent capacity assessments and determine if the potential participant can provide legally effective informed consent. Documentation of this training should be retained by the investigator.
- Will ensure that an assessment of a potential participant's capacity to consent is conducted during the consent discussion and that participation in the research is based on an adequate understanding of the study. The assessment of capacity to provide consent is required regardless of risk. The individual who is responsible for determining whether a potential participant has the capacity to consent must have appropriate expertise necessary to make such a determination and must also monitor the participant's ability to voluntarily continue to participate in the research.
- Will ensure, when applicable, that an independent assessor is present during assessment of a potential participant's capacity to consent. Inclusion of an independent assessor, e.g. an unaffiliated clinician or subject advocate, may be necessary to mitigate the potential for coercion or conflict of interest. An independent assessor must have no affiliation with the study or the sponsors of the study. The investigator must document use of an independent assessor within the study files and/or per departmental practice.
- If an independent assessor is involved in the consent process, the assessor will provide a report outlining the outcome of each potential participant's initial

assessment of capacity to consent. The investigator is responsible for submitting this report of the assessor's findings to the IRB as part of the study's continuing review.

- To avoid therapeutic misconception, the following language should be added to the informed consent document: "Your healthcare provider may be referring you to this research study. If your healthcare provider is also an investigator on this study, there is the chance that his or her responsibilities for the study could influence his or her recommendation for your participation. If you prefer, your healthcare provider will be happy to refer you to another investigator on the research study team for you to decide if you want to participate in the study and to see you for the research study activities while you are in the study".

IRB Responsibilities

When reviewing protocols planning to enroll participants who may have impaired consent capacity, or drawing research participants from a population likely to have impaired consent capacity, the IRB:

- Will consider the investigator's justification for inclusion of individuals who lack consent capacity in terms of ethical appropriateness and scientific necessity for the proposed study, consider the extent to which the scientific questions posed by the research are answerable in those who have the capacity to consent, and determine that the relationship of risks to benefits is reasonable.
- Will consider whether one or more individuals who are knowledgeable about or experienced in working with individuals with impaired consent capacity should be included in the review of the protocol.

Per 45 CFR 46.107 and 21 CFR 56.107: "An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB". This may include involvement of:

- medical/scientific experts;
- patient advocates;
- experts in the assessment of consent capacity and/or experts with knowledge of the scientific, legal, regulatory, and ethical issues.
- Will require protections and additional safeguards proportional to the expected severity of consent capacity impairment in potential participants, magnitude of experimental risk, anticipated benefits to the subject and/or society, complexity of the study design, and other relevant factors. More frequent IRB review may be needed throughout the course of the study. Per 45 CFR 46.111(b) and 21 CFR 56.111(b): "When some or all of the subjects are likely to be vulnerable to coercion or undue influence, including those with cognitive limitations, the IRB must be sure that additional safeguards have been included in the study to protect the rights and welfare of these subjects".
- ***When applicable**, will evaluate the role of the LAR in the consent process and consider applicable laws.

***Refer to** "Guidance for Investigators and the IRB: Informed Consent and Assessment of Capacity to Consent to Research", item #1 under the

heading “IRB responsibilities when reviewing protocols planning to enroll participants with impaired consent capacity”.

- *May require inclusion of an independent assessor during initial assessment of a potential participant's capacity to consent as well as during the informed consent process. An independent assessor must have no affiliation with the study or the sponsors of the study.

***Refer to** “Guidance for Investigators and the IRB: Informed Consent and Assessment of Capacity to Consent to Research”, item #2 under the heading “IRB responsibilities when reviewing protocols planning to enroll participants with impaired consent capacity”.

- Will evaluate methods described by the investigator for re-evaluating participant’s capacity to consent over the course of the study. See section titled “Fluctuating Consent” within this policy.
- Will consider procedures described by the investigator for obtaining the assent of adult participants who cannot consent when the individual is capable of generally understanding the nature of participation in a research study and capable of communicating.

Fluctuating Capacity

For research involving individuals who are able to provide informed consent, but are expected to have fluctuating, limited, or diminishing decision-making capacity during the course of the research study, special processes or procedures must be outlined in the study protocol to ensure that the rights and welfare of such individuals remain adequately protected. These processes could include the timing of study procedures to avoid periods of heightened vulnerability where possible, advance directives to document the participant’s intent and attitude toward research participation at the time the research participant is capable of decision-making, or the use of an independent monitor. Investigators must establish and maintain ongoing communications with involved caregivers, consistent with participant autonomy and with medical confidentiality.

Individuals who exhibit temporarily impaired consent capacity due to environmental or other factors (i.e., women in advanced and active labor, individuals under the influence of drugs or alcohol, individuals in extreme emotional or physical distress) should not be asked to provide informed consent for research until they regain their decision-making ability. Individuals who have received medication for the purpose of minimal, moderate, or deep sedation, as defined in the Mayo Clinic “Sedation Policy”, should not be asked to provide informed consent for research until they regain their decision-making ability. (See link below in “References and Resources” to the Mayo Clinic “Sedation Policy”). However, in the event that the research is designed to study individuals in these situations, or the study plan necessitates approaching potential participants at that time, the study design must employ additional safeguards such as involvement of a family member or LAR in the consent discussion, and arrange for the participant to meet with the study team once the situation has passed to confirm comprehension and continued voluntary participation in the study. Whenever practical, investigators should design the research so that participants will be appropriately consented and enrolled prior to any temporary decisional impairment.

Surrogate Consent

No investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative (45 CFR 46.116 and 21 CFR 50.20)

Surrogate consent is obtained from the participant's legally authorized representative (LAR). (See link below in "References and Resources" to the Mayo Clinic IRB policy "Selecting a Legally Authorized Representative".

Research which contemplates enrolling participants who are not able to provide informed consent and proposes to obtain LAR consent must be approved by the IRB. When the individual is capable of generally understanding the nature of participation in a research study and capable of communicating, assent should be sought from the participant. Where assent is sought, mere failure to object may not be construed as assent. Any meaningful objection by the potential participant regarding study participation must be taken as a refusal or withdrawal and be honored, even if the LAR or the person obtaining consent disagrees with the decision. (Note: This statement does not apply to studies enrolling pediatric participants where parents may, under specified regulatory circumstances, overrule a child's objection). However, for some studies, withdrawal may require continuation of some research interventions to protect participant safety and well-being. Withdrawal consequences must be specified in the consent document(s).

Studies NOT planning to enroll participants who may have impaired consent capacity

- *A study that did not specifically plan to enroll individuals lacking capacity to consent may encounter a potential participant where the study team is unsure if the potential participant has the capacity to provide informed consent. The study team is responsible for assessing the potential participant's capacity to consent and/or contacting the Research Subject Advocate (RSA) or the Research Compliance Office to serve as an independent assessor.
- If it is determined that the potential participant does not have the capacity to provide informed consent, the investigator must either exclude the potential participant from enrollment to the study or seek surrogate consent for participation. Inclusion of a legally authorized representative for the use of surrogate consent requires submission of a protocol modification for review and determination by the convened IRB.
- In time-sensitive situations where delay of enrollment to allow review of the modification by the convened IRB may not be in the best interest of the participant, the study provides the potential for benefit to the participant, and the participant is not subject to protections by the federal regulations under 45 CFR 46 Subpart B (Pregnant Women, Human Fetuses and Neonates), and/or Subpart C (Prisoners):
 - a. The investigator should submit a modification via IRBe requesting the use of a legally authorized representative for a single participant. The modification should include justification for inclusion of the participant and confirmation by the investigator that the study provides the potential for benefit to the participant. The modification should also include a revised consent form adding signature lines for the legally authorized

representative, and revision of the IRBe application to include completion of the sections titled “Protected Study Populations” and “Adults Lacking Capacity to Consent”.

- b. Contact the IRB Service Center and ask to speak to an IRB Operations Coordinator regarding the inclusion of a legally authorized representative for a single participant.
- c. The IRB Operations Coordinator will consult with an IRB Chair to assess the modification via the expedited review process.
- d. The enrollment process may proceed if the investigator receives IRB approval of the modification and when an approved consent form has been issued by the IRB.

***Refer to** “Guidance for Investigators and the IRB: Informed Consent and Assessment of Capacity to Consent to Research” item #3 under the heading “Studies NOT planning to enroll participants with impaired consent capacity”.

Re-reviewing Research When an Adult Participant Unexpectedly Loses the Capacity to Consent

- *A participant in a study that does not have IRB approval to include participants lacking capacity to consent may unexpectedly experience a substantial impairment to his or her functional abilities that is not foreseeably temporary. In this case, researchers should notify the IRB and the IRB should determine whether the participant is permitted to remain in the study. Re-review of research should follow the procedures specified within this policy. If the participant is determined to be incapable of consenting and is not likely to regain the capacity to consent in the near future, but the IRB determines that his or her ongoing participation is reasonable, researchers should obtain the participant’s assent to continue in the study as well as obtain the consent of an LAR.

***Refer to** “Guidance for Investigators and the IRB: Informed Consent and Assessment of Capacity to Consent to Research”, item #4 under the heading “Re-reviewing Research When an Adult Participant Unexpectedly Loses the Capacity to Consent”.

Related Procedure(s)

N/A

Related Document(s)

N/A

Definitions

Consent Capacity: An individual’s ability to understand and process information relevant to making an informed, voluntary decision to participate in research. Several kinds of information are crucial to such decisions, including an understanding of the purpose of the study, its experimental nature, risks and anticipated benefits, the right to withdraw, alternatives to participation, confidentiality protections, and the safeguards used to minimize risks. A wide variety of diseases, disorders, conditions, situations, and injuries can affect a person’s ability to understand such information, to weigh the

advantages and disadvantages of participation in research, and to reach an informed decision regarding study participation.

Consent Document: A structured, written description in understandable terms of relevant research project information. The consent document is not consent itself; it is the record of what has been communicated to a potential participant. It is the document that ensures all regulatory elements are present and communicated to a potential participant. When signed by the potential participant, the consent document is a record of the receipt of research-related information by the participant. It also serves as reference material for the participant as the research project progresses. It is not a contract and is not legally binding, and the participant may choose to withdraw consent at any time.

Enrollment: Occurs when an eligible, informed, potential participant undergoes the initial informed consent process and voluntarily agrees to participate in a research project. Example: You enroll 100 to accrue 25. See also Accrual.

Fluctuating Capacity: Capacity to consent may alter as a function of the natural course of an illness, response to treatment, effects of medication, general physical health, and other factors. Therefore, a participant's ability to provide ongoing informed consent must be re-evaluated periodically throughout the course of his or her participation in a study.

Impaired Consent Capacity: Impaired consent capacity may involve partial impairment, impairment that fluctuates over time, or complete impairment. For example, consent capacity can be affected by a wide range of disorders and conditions, such as dementia, stroke, traumatic brain injury, developmental disorders, serious mental illness, intoxication, and delirium.

Informed Consent: An ongoing process of communication between the participant and the study team. Informed consent is a continuing process by which a participant, after having been informed, voluntarily confirms his or her willingness to participate in a research project and can demonstrate understanding of all aspects of the research project that are relevant to the participant's decision to participate.

Legally Authorized Representative (LAR): A legally authorized representative (LAR) is defined in both HHS and FDA regulations as an individual or judicial or other body authorized under applicable law to consent on behalf of a potential participant to participation in the procedure(s) involved in the research (45 CFR 46.102(c) and 21 CFR 50.3(1), respectively).

State law may define when an LAR may be appointed and who may serve in this capacity on behalf of another. Executing a Durable Power of Attorney (DPA) for health care, which is an authorization that one person gives to another to act on his or her behalf, is one method to identify an LAR. Alternatively, many states have statutes to clarify when and which family members may serve as LARs.

Legally Effective Informed Consent: A potential participant has been provided enough information to make a decision; the potential participant has the capacity to make a decision; the potential participant understands the consequences of his or her decision; and the potential participant can communicate that decision.

Surrogate Consent: Consent obtained from the participant's legally authorized representative (LAR).

Therapeutic Misconception: The term "therapeutic misconception" is used to describe the assumption by research participants that decisions about their care are being made

solely with their benefit in mind. Therapeutic misconception can be defined as the situation where a participant or a LAR either overestimates the direct therapeutic benefits which may be gained by participation in the research and/or underestimates the risks thereby compromising their ability to provide and/or maintain a voluntary and knowing informed consent.

Investigators must be especially careful to make participants and their families or caretakers aware of the differences between individualized treatment versus research and the separate and distinct roles of the clinician and the research investigator.

Vulnerable Populations in Research: Vulnerable populations may include (but are not limited to): individuals who are pregnant; prisoners; individuals who have been involuntarily committed to a medical facility; children; subordinates such as students, trainees, and employees; individuals who are economically or educationally disadvantaged; individuals who have a language barrier; individuals with a cognitive disability; and individuals with an illness for which all standard treatment options have been exhausted. Federal regulations state that “when some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects”. (45 CFR 46.111(b) FDA regulations expressly identify "mentally disabled persons" as a vulnerable category of subjects in clinical investigations for which IRBs may need to assume increased responsibilities. (21 CFR 56.107(a) and 56.111(b).)

References

Association for the Accreditation of Human Research Protection Programs (AAHRPP):
Reviewing Research Involving Adult Participants with Diminished Functional Abilities
Related to Capacity to Consent

www.aahrpp.org

Appelbaum, PS, and Grisso, T: MacArthur Competence Assessment Tool for Clinical Research (MacCATCR), Professional Resource Press, Law and Psychiatry Program, University of Massachusetts Medical School, Worcester, MA, 2001.

Appelbaum, PS, and Candilis, PJ: A Direct Comparison of Research Decision-making Capacity: Schizophrenia/Schizoaffective, Medically Ill, and Non-III Subjects, 2009

Cullen et al. (2007). “A review of screening tests for cognitive impairment.” *Journal of Neurology, Neurosurgery & Psychiatry*, 78: 790-9;

Dunn et al. (2006). “Assessing decisional capacity for clinical research or treatment: a review of instruments.” *American Journal of Psychiatry*, 163: 1323-34;

Food and Drug Administration (FDA): Informed Consent Information Sheet: Guidance for IRBs, Clinical Investigators, and Sponsors

<http://www.fda.gov/RegulatoryInformation/Guidances/ucm404975.htm>

Jeste DV et al. (2007). A New Brief Instrument for Assessing Decisional Capacity for Clinical Research. Arch Gen Psychiatry 64(8):966-74.

Minnesota Commitment and Treatment Act (2009)

National Institutes of Health: Research Involving Individuals with Questionable Capacity to Consent <http://grants.nih.gov/grants/policy/questionablecapacity.htm>

Sturman ED. (2005) *The Capacity to Consent to Treatment and Research: A Review of Standardized Assessment Tools*. *Clinical Psychology Review*. 25:954-974

[45 CFR 46](#)

[21 CFR 50](#) and [56](#)

The Belmont Report: <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html>

Mayo Clinic IRB Policy "Informed Consent and the Research Subject"
<http://mayocontent.mayo.edu/irb/DOCMAN-0000047834>

Mayo Clinic IRB Policy "Special Categories of Research: Vulnerable Human Subjects Policy"
<http://mayocontent.mayo.edu/irb/DOCMAN-0000047857>

Mayo Clinic IRB Policy "Selecting a Legally Authorized Representative"
<http://mayocontent.mayo.edu/irb/DOCMAN-0000047848>

Mayo Clinic Policy "Informed Consent for Procedures Policy"
<http://mayocontent.mayo.edu/prmr/DOCMAN-0000156110>

Mayo Clinic Policy "Moderate Sedation Policy"
<http://mayocontent.mayo.edu/anesthesiology/DOCMAN-0000200974?qt=sedation>

Mayo Clinic Legal Department website
<http://mayoweb.mayo.edu/legal/research.html>

Mayo Clinic IRB "Guidance for Investigators and the IRB Informed Consent and Assessment of Capacity to Consent to Research Policy"
<http://mayocontent.mayo.edu/irb/DOCMAN-0000197845>

Informed Consent for Research: A Guide to Assessing a Participant's Understanding
<http://intranet.mayo.edu/charlie/irb/child-of-page-1/forms-library/>

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Revision History

Date	Synopsis of Change
October 18, 2017	1) Added to 4th bullet under Investigator Responsibilities: including methods for consenting at the time participant regains capacity, as applicable. 2) Under References, added Moderate to Sedation Policy; and added Policy to Guidance for Investigators and the IRB Information Consent and Assessment of Capacity to Consent to Research Policy. 3) Updated Enrollment definition per Glossary review.

August 31, 2017	Updated the Mayo Clinic Policy "Sedation Policy" with the link that Angie provided in her note of 7/31/17.
May 16, 2017	Scheduled review. Moved content into the policy template. Under References: changed title from 'Special Categories of Research: Participants Who May Be Vulnerable to Coercion or Undue Influence' to 'Special Categories of Research: Vulnerable Human Subjects Policy'; and fixed broken link for Mayo Clinic Legal Department website, remove 'whether it is necessary to re-evaluate the participant's capacity to consent and to determine' from 1st bullet under heading 'Re-reviewing Research When an Adult Participant Unexpectedly Loses the Capacity to Consent'; hyperlinked 45 CFR 46 and 21 CFR 50 and 56; and changed Paterson LaBaw to Paterson.
4/14/2016	Addition of process for expedited review of modifications requesting inclusion of a legally authorized representative for a single subject.
1/5/2016	New Document