Scope

This policy defines the heightened safeguards that all researchers must employ in order for a Yale Institutional Review Board (IRB) to approve the participation of adult individuals with impaired consent capacity in biomedical, behavioral, and social science research.

Policy Statement

IRBs and investigators must operate according to the principles that individuals with impaired consent capacity who are recruited for or enrolled in research studies must be treated in a manner commensurate with their special status. Research involving these individuals should employ additional safeguards as appropriate to the study and the participant population in order to protect their rights and welfare.

Reason for the Policy

It is important, necessary, and in keeping with the Belmont principles of beneficence and justice to include individuals with impaired consent capacity as participants in research projects. A number of conditions associated with decisional impairment, such as stroke and Alzheimer’s disease, afflict ever-increasing numbers of individuals in society and impose growing burdens on those individuals, their families, and society. Scientifically and ethically appropriate research involving these individuals is critical to illuminate the underlying disease mechanisms that lead to these conditions and to identify promising treatments. To be most useful and free of bias, that research must include individuals with severe and chronic forms of these disorders as well as those exhibiting minimal impairment. Engaging individuals in research who cannot consent for themselves or whose decision-making capacity may be compromised or may fluctuate over time may result in their inability to protect their own self-interests. Therefore, additional safeguards must be implemented, as required in 45 CFR §46.111(b) and 21 CFR §56.111(b) and described herein (see Procedure 340 PR.1 Assessment of Capacity to Consent for additional information).

Definitions

Assent
An individual’s affirmative agreement to participate in research. This should be sought in addition to the consent of a legally authorized representative or surrogate when the individual is sufficiently cognitively capable of understanding the nature of his or her participation in a research study. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Impaired Consent Capacity
A compromised capacity to understand information related to the research and to make a reasoned decision about initial or continuing participation in research that may preclude the individual from providing legally effective
consent. Such impairment or compromised capacity may be temporary, permanent, or may fluctuate. Examples of individuals who may have impaired consent capacity include women in active labor, individuals who have suffered a stroke or other acute and severe illness, individuals under the influence of drugs or alcohol, individuals experiencing considerable pain, individuals under extreme emotional distress (e.g., learning of a newly diagnosed life threatening or terminal illness for self or loved one, anticipating imminent major surgery), and individuals suffering from cognitive disorders or mental disorders. Impaired consent capacity as defined in this policy is distinct from legal incompetence.

**Legal Incompetence**
A designation of status that has been adjudicated in a court proceeding, and often referring to an inability to manage one or more significant areas of life such as business or monetary affairs. Although an individual may be designated as legally incompetent, he or she does not automatically have impaired consent capacity in terms of consenting to research. Similarly, an individual may be legally competent, but still have impaired consent capacity in terms of providing consent to participate in a research study.

**Legally Authorized Representative (LAR)**
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. An LAR is authorized through a legal process and has documentation of that designation.

**Research Advance Directive**
A document used to indicate willingness to continue to participate in a research study or in future studies. In filling out an advance directive, the participant, who at the time is capable of consenting, provides consent to document his/her willingness to continue to participate in the research study in the future or in other future studies during which it is likely that the participant will not be capable of providing consent. An advance directive may also be used to allow the participant to name an individual that the participant would like to act as his/her surrogate to provide permission for the participant’s continuation in a current study or enrollment in a future study, in addition to the participant’s assent. (See Research Advance Directive template at [http://www.yale.edu/hrpp/forms-templates/biomedical.html](http://www.yale.edu/hrpp/forms-templates/biomedical.html) ) Advance directives, with surrogate appointments should be considered in studies which investigate subjects over time and involve the potential for a decline in capacity to give ongoing consent to participate or in those studies in which alteration of consciousness is likely to occur during the course of the study.

**Surrogate Permission**
Permission for an individual to participate in research given by an appropriate surrogate (e.g., next of kin – spouse, parent, child, sibling) when an individual is assessed as not capable of providing fully informed and legally effective consent.

**Therapeutic Misconception**
An individual's belief that research studies are intended to benefit the participants who enroll in them and that the individual is being asked to participate in a research trial as part of his or her clinical care even after adequate and repeated information and explanations about the risks and benefits of the study have been provided.

**Policy Sections**

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340.1 IRB Considerations
IRBs reviewing projects involving adult participants with impaired consent capacity must include one or more members or consultants who are familiar with the conditions that may affect the prospective participant’s capacity to provide consent and with the concerns of the population being studied. IRBs should consider whether it is necessary to consult with or to have in attendance a special representative familiar with the disorder and capable of addressing concerns specific to the subject population (45 CFR §46.107(a); 21 CFR §56.107(a)).

The IRB will approve research projects which propose to include individuals with impaired consent capacity only after consideration of safeguards in addition to the requirements for approval described in the IRB Review Policy. (See [340 CH. 1, Impaired Consent Capacity Checklist](http://www.yale.edu/hrpp/forms-templates/biomedical.html))
**Appropriateness of Inclusion**
Individuals who have been found to have impaired consent capacity may be enrolled in research only when the IRB finds that their participation in the study is justified, there is a sufficient plan for obtaining and continually assessing assent, and appropriate additional safeguards are in place to protect them, such as, where appropriate and feasible, provisions for surrogate permission or an advance directive.

Furthermore, the IRB must find that their participation in research:

- Presents no more than minimal risk; or
- Presents greater than minimal risk, provided that IRB finds that:
  - The risks are justified given the potential benefits of the research either to the participants or to the development of generalizable knowledge to benefit the participants’ class of individuals.

**Justification for Inclusion**
Whenever possible, research should be designed to include only those individuals who are capable of consenting for themselves. In some studies, however, where benefit is likely, it is more ethical and in line with the Belmont principles to include individuals with impaired consent capacity. In other studies, even those without potential (or likely) benefit to participants, the only way to answer the scientific aim may be to include such individuals in the research.

Investigators proposing research targeting adult individuals with impaired consent capacity as participants must provide IRBs with a thorough justification for their proposed research design, including how capacity will be assessed, plans to include surrogate permission, plans for assessing subject assent (where appropriate) and a description of the procedures that are designed to minimize risks and discomfort to participants. IRBs must consider whether the protocol includes a reasonable rationale for inclusion of individuals with impaired consent capacity as a target population.

**Risk:Benefit Assessment**
A research study specifically designed to include individuals with impaired consent capacity must have as its goal either to study treatment designed to directly benefit the individual, or the development of important generalizable knowledge regarding the disease or condition of the targeted population that includes a substantial portion of individuals with the same impaired capacity as the subjects. The IRB’s deliberations shall include consideration of the nature and degree of anticipated impairment of the targeted study populations, the risk level of the proposed study, and the potential for direct benefit to the study participants.

**340.2 Investigator Obligations**

**Requisite Expertise**
The investigator must ensure that the individual who is responsible for determining whether a potential participant has the capacity to consent has the appropriate expertise necessary to determine and monitor the participant’s capacity initially and on an ongoing basis. The determination is made by individual observation of and interaction with the potential participant. The determination may be made by an investigator or by another professional who has appropriate expertise. It may also include opinions from one or more caregivers.

**Assessment of Capacity to Provide Consent**
Research studies designed to involve individuals with impaired consent capacity must include a means to assess a potential participant’s capacity to provide consent and the criteria for identifying individuals who are impaired. At a minimum, this assessment must include a method to evaluate the potential participant’s ability to understand the relevant study information, e.g., the nature of the research and its likely consequences, to process information about the research rationally, and to communicate a choice clearly as to whether or not he/she wishes to participate.
1. For research contemplating enrolling participants who are not able to provide informed consent at the outset of the study, and where an advance directive is not possible due to their condition, permission from a surrogate for their participation must be approved by the IRB (see Policy 200, Informed Consent for Human Research).

2. Assent must be sought when the individual is sufficiently cognitively capable of understanding the nature of his or her participation in a research study and capable of communicating. Where assent is required, mere failure to object may not, absent affirmative agreement, be construed as assent.

**340.3 Surrogate or Legally Authorized Representative**

Absent a participant-designated or state-specified legally authorized representative (LAR) for research decision-making, investigators may engage and IRBs may approve as surrogates individuals who are specified in state statutes as LARs for medical decision-making or, in the absence of such statutes, individuals who would normally provide consent for medical care under prevailing, commonly accepted clinical practices. Participant assent also must be obtained whenever possible.

The IRB shall consult with Institutional legal counsel regarding the categories of surrogates eligible to serve as LARs in different situations.

The IRB shall adhere to Connecticut state statutes that explicitly prohibit court-appointed guardians of mentally retarded individuals from giving permission for their wards to participate in research unless certain stringent terms and conditions are met (CGS § 45a-677(e)).

**340.4 Additional Safeguards**

The IRB may require additional safeguards depending on the protocol and the level of potential risk to the participants involved. Such safeguards may include the use of an independent monitor and/or assessor; special informational or educational techniques; or the use of waiting periods to afford participants and their surrogates more time to decide about participation.

**Related Information**

340 PR.1  Assessment of Capacity to Consent

340 CH 1  Points to Consider: Studies Involving Participants with Impaired Capacity to Consent

Federal Regulations: 45 CFR §46.111(b); 21 CFR §56.111(b); 45 CFR §46.107(a); 21CFR §56.107(a)

Connecticut State Statutes: CGS §45a-677(e)
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<tbody>
<tr>
<td>Research Studies involving Individuals with Impaired Consent Capacity</td>
<td>Human Investigation Committee or Human Subjects Committee</td>
<td>(203) 785-4688 <a href="mailto:ysmhic@yale.edu">ysmhic@yale.edu</a> <a href="mailto:human.subjects@yale.edu">human.subjects@yale.edu</a></td>
</tr>
<tr>
<td>Surrogate or Legally Authorized Representative</td>
<td>Office of the General Counsel</td>
<td>(203) 432-4949</td>
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Roles and Responsibilities

**Human Research Protection Program**

The Human Research Protection Program (HRPP) is responsible for oversight of human research protection through ongoing education, monitoring and evaluation of all parties involved in the conduct of human research.

**Human Investigation Committee (HIC)**

HIC I, HIC II, HIC III and HIC IV serve as the four Institutional Review Boards or IRBs for biomedical human research conducted at Yale University.

**Human Subjects Committee (HSC)**

The HSC serves as the Institutional Review Board for social, behavioral and educational human research at Yale University.

**Office of the General Counsel (OGC)**

The OGC serves as legal advisor to the Yale community.

Revision History

1/8/2009, 9/26/2012