INSTITUTIONAL REVIEW BOARD REVIEW OF 
RESEARCH INVOLVING COGNITIVELY IMPAIRED INDIVIDUALS

DESCRIPTION

Research participants may have cognitive impairment due to developmental disabilities, psychiatric or medical condition, or other reason. The impairment may be chronic or transient. Regardless of the reason or duration of decisional impairment the University of Cincinnati (UC) Institutional Review Board (IRB) shall ensure that appropriate additional protections are provided so the rights and welfare of this population are maintained.

COGNITIVELY IMPAIRED INDIVIDUALS

- Includes individuals who have decisional impairments, including but not limited to the following.
  - Developmental disability (e.g. mental retardation)
  - Psychiatric diagnosis (e.g. schizophrenia)
  - Dementia (e.g. Alzheimer's disease)
  - Stroke or other medical diagnosis or condition that causes cognitive limitation.

- Includes individuals who are transiently cognitively impaired, including but not limited to the following.
  - Use of a substance that impairs cognition (e.g. some drugs, alcohol)
  - Trauma patients
  - Surgical patients

- Requires the researcher to be alert to changes in cognition that may affect the participant's willingness to continue in the research or may require obtaining permission from the participant's surrogate for continued participation.
RESPONSIBILITY

The IRB Chair or designee shall determine whether or not cognitively impaired individuals will be recruited as participants in a research study and, if so, shall ensure that review processes described in Human Research Protection Program (HRPP) Policy V.01 Protecting Vulnerable Populations in Human Subject Research are followed.

Human Research Protection (HRP) staff shall ensure that required documentation is maintained in the IRB's study records and meeting minutes.

PROCESS

DEFINITIONS

Assent: The agreement of a person who cannot provide legally effective informed consent to participate in research. It is usually obtained in conjunction with permission from the individual's Legally Authorized Representative (LAR). Mere failure to object should not be construed as assent.

Cognitively or Decisionally Impaired: Having a psychiatric disorder (e.g. psychosis, neurosis, personality or behavior disorder), organic impairment (e.g. dementia), or a developmental disorder (e.g. mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including individuals under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and individuals with severely disabling physical handicaps may also be compromised in their ability to make decisions in their best interest.

Community Advisory Committee (CAC): A committee established by the UC College of Medicine Department of Psychiatry that includes members of communities in the UC area who have an interest in psychiatry research that may impact the community.

Durable Power of Attorney for Healthcare (DPAHC): A power of attorney that appoints a health care agent that remains in effect if the principal becomes incapacitated.

Legally Authorized Representative: An individual, judicial, or other body authorized under applicable law to grant permission on behalf of a prospective participant for their participation in research activities.
Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Next of Kin: A person's closest living blood relative or relatives in the following order of priority, unless otherwise specified by applicable law: spouse, adult child (18 years of age or older), parent, adult sibling (18 years of age or older), grandparent, or adult grandchild (18 years of age or older). If there are two surrogates of the same level (for example, two adult children) who disagree with regards to the subject’s participation then the subject will not be permitted to be enrolled.

Surrogate Consent: Permission obtained from an individual's LAR for the individual to participate in a research study. The surrogate's responsibility is to determine what the subject would decide if competent, or if the subject's wishes are not known, what they think would be in the subject's best interest. In Ohio only the DPAHC, the LAR and the Next of Kin, in that order, may give surrogate consent for research participation. In this Procedure, "LAR" and "surrogate" include the DPAHC and Next of Kin unless specifically stated otherwise.

CONSIDERATIONS

1. Does the scientific or scholarly design of the study require inclusion of this vulnerable population?

   Cognitively impaired persons must not be recruited for research simply because they are readily available. There must be a compelling reason to include them in the research study.

2. Is it likely that some participants may become cognitively impaired during their study participation? If so, are appropriate procedures included to obtain surrogate consent before their cognitive ability becomes impaired?

3. Are there risks of coercion or harm to the study's participants that are related to being decisionally impaired?

4. Will the vulnerable population receive direct benefit from participating in the research?
5. Are the population-specific risks reasonable in relation to the anticipated benefits?

Cognitively impaired persons will not be participants of research that imposes a risk of injury unless that research is intended to benefit that subject and the probability of benefit is greater than the probability of harm.

6. Are protections adequate to avoid coercion during recruitment and consenting of this vulnerable population? Are LARs appropriately included in the recruitment and consenting processes?

The LAR must be given descriptions of both proposed research study and the obligations of the person’s representatives. Disclosures required by the IRB to be made to the subject by the investigator must be made to the subject’s surrogate.

If feasible, in addition to surrogate consent, the investigator should attempt to explain the proposed research to the prospective research subject and obtain the subject's assent. Some persons may resist participating in a research protocol that has been approved by their representatives. Under no circumstances may participants be forced or coerced to participate.

The IRB may waive the consent requirement under the federal regulations allowing for waiver of consent after consideration and comment by the local community on the research. See HRPP Policy II.01 Obtaining Informed Consent in Human Subjects Research and HRPP Procedure 202 Exception from Informed Consent in Clinical Research.

7. Are participants able to give documented assent, using an appropriate simplified Assent form? Is it necessary to document the subject's comprehension during the consenting process? If documented assent will be sought, documented permission of the LAR usually also will be required.

8. Are these vulnerable participants able to withdraw from the study without penalty, undue influence to remain in the study, or loss of benefits they would otherwise have?

REQUIREMENTS OF IRB REVIEW

1. IRB Membership Requirements

   a. The IRB roster shall include at least two members who are familiar with the population to be recruited. One member who is familiar with the population to be
recruited must be from the CVAMC when CVAMC research involving cognitively impaired participants is reviewed. Consideration may be given to adding a member of the population or a family member of such a person or a representative of an advocacy group for that population.

b. The IRB shall utilize outside consultant(s) as necessary to assure appropriate expertise as described in HRPP Procedure 305 Inviting Consultants to Review Institutional Review Board Protocol Documents. Such ad hoc members may not vote with the IRB or contribute to the quorum.

2. Additional Considerations

a. Both investigators and IRB members must be aware that for some participants, their decision-making capacity may fluctuate.

i) A subject who regains the cognitive ability to consent must be re-consented using standard consenting procedures.

ii) The investigator may determine after appropriate medical or psychological evaluation that the prospective research subject lacks decision-making capacity and is unlikely to regain it within a reasonable period.

b. The IRB may require monitoring of the consent process, the use of a consent comprehension tool, discussion with family members of the participant, or other measures the IRB believes may protect the rights and welfare of vulnerable participants.

c. Consenting is an ongoing process. All applicable criteria that would trigger re-consenting a subject in any study shall apply to re-consenting surrogates who have given consent for an individual with cognitive impairment. It may also be appropriate to explain the changes to the impaired participant to obtain continuing assent.

d. In the event a subject has been initially consented by a surrogate, and a surrogate of higher priority subsequently notifies the investigator of that relationship to the subject, the investigator must defer to the higher priority surrogate's decision regarding whether the subject will continue to participate or to withdraw from the study.
REQUIREMENTS OF RESEARCH CONDUCTED AT CVAMC

When research involves the Cincinnati Veterans Administration Medical Center (CVAMC), additional protections or restrictions will apply as described in the VHA Handbook 1200.5, Appendix D

Per Medical Memorandum 151-2, Paragraph II.F.2, regarding surrogate consent, “such consent may be requested and accepted only when the prospective research participant is incompetent or has impaired decision-making capacity as determined and documented in the person’s medical record in a signed and dated progress note.”

INDIVIDUALS WITH A PSYCHIATRIC DIAGNOSIS

Generally, individuals with a psychiatric diagnosis are able to participate in research if, in the judgment of the researcher, the individual is able to comprehend that he/she is participating in research, understands the risks and benefits of the research, and is able to give an informed consent. However, there are additional protections required for certain individuals who are able to consent but may be vulnerable to coercion.

1. If a patient is hospitalized with a psychiatric diagnosis, the individual may provide his or her own consent to participate in research if it is documented that the individual is competent to participate in informed consent process.

2. Consultation with a psychiatrist or licensed psychologist who is not involved in the research activity must be obtained if it is determined that a prospective research subject may lack the decision-making capacity due to a psychiatric illness.

3. A study must first be reviewed and approved by the CAC if the study:
   a. Involves more than minimal risk; and
   b. Involves outpatients with diagnoses of schizophrenia, schizoaffective disorder, or bipolar disorder, or major depressive disorder; and
   c. Includes a placebo that is not combined with an active medication (i.e., a placebo alone) for any period of time during the course of the study.
   d. The UC IRB must have documentation of review of the research by the CAC, including the total vote count. If some CAC members opposed the study, those members shall be given the opportunity to attend a UC IRB meeting to explain the
grounds for their opposition. They may not be present in the meeting for the balance of the discussion or voting.

DETERMINATIONS REQUIRING DOCUMENTATION

1. 45 CFR 46.111(a) Selection of subjects is equitable.

   The investigator must demonstrate to the IRB that there is a compelling reason to include cognitively impaired participants.

2. 45 CFR 46.111(b) Additional safeguards have been included to protect the rights and welfare of participants.

   Cognitively impaired persons will not be participants of research that imposes a risk of injury unless that research is intended to benefit that subject and the probability of benefit is greater than the probability of harm.

3. 45 CFR 46.116 Informed consent must be obtained from the subject or the subject's LAR.

   Surrogate consent must be obtained. LARs must be given descriptions of the obligations of a representative to determine what the subject would do if competent or what they think is in the incompetent person's best interest.

   For research involving participants whose ability to comprehend may fluctuate, the IRB may require that participants involve family members or caregivers in the consent process and may require periodic re-consent.

   The IRB may require an appropriate method of assessing the decision-making capacity of potential participants.

ADDITIONAL CONSIDERATIONS REGARDING INFORMED CONSENT

The ability of individuals to participate in research if they are unable to consent depends on the law of the state where the research is being conducted. If the site of the research is outside Ohio, the researcher must provide a legal opinion acceptable to the IRB of the circumstances under which the law of the state where the research is conducted allows individuals who do not have the capacity to consent to participate in research.
Applicable regulations, Document(s):
21 CFR 50 Subpart B
45 CFR 46.111
45 CFR 46.116
45 CFR 46.117

Checklist for Principal Investigators to Complete Regarding Research Involving Participants Who Are Cognitively Impaired
Policy I.01 Composition of the Institutional Review Board
Policy II.01 Obtaining Informed Consent in Human Subjects Research
Procedure 202 Exception from Informed Consent in Clinical Research
Procedure 305 Inviting Consultants to Review Institutional Review Board Protocol Documents
VA Handbook 1200.5
VA Medical Memorandum 151-2, Paragraph II.F.2

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<td>6/2014</td>
<td>C. Norman</td>
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<td>New Procedure to replace Policy V.06 (Cognitively Impaired) and Policy V.07 (Psychiatric Diagnosis) and include excerpted language from Procedure 308 regarding cognitively impaired participants, including revisions to wording and formatting for clarity and to be consistent with other Procedures.</td>
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Date: June 2014
Signature signed copy on file