Human Research Protection Program Departmental Policy and Procedure

2.6 Research Involving Individuals With Diminished Autonomous Decision-Making Capacity

Responsible Office: Human Research Protection Program Department (HRPPD)

Effective Date: September 3, 2026

I. Policy Statement

a. The Institutional Review Board (IRB) gives special consideration to protecting the rights and welfare of individuals with diminished autonomous decision-making capacity (DADMC). The IRB regards protections from coercion, undue influence, manipulation and physical control as critically important to protecting human subjects. DADMC refers to a person with limits in either **mental capacity** or **voluntariness**. Research involving individuals with DADMC is permitted if the IRB finds that it is appropriate and that sufficient safeguards have been incorporated into the protocol to protect the subjects.

b. Presumption of capacity: Subjects with diminished autonomous decision-making capacity who have not been documented to have impaired decision making (by medical documentation), to be incapacitated (by medical or legal documentation) or to be incompetent (by legal documentation), are to be considered capable of giving informed consent for research unless and until IRB approved plans to assess mental capacity reveal otherwise.

c. The following populations are routinely considered to have DADMC due to regulation, policy, or circumstance:

   i. Those with limited mental capacity that require consideration of additional protections:

      1. Children,

      2. Individuals with impaired decision-making capacity, and

      3. Incompetent or incapacitated individuals.

4. Mentally handicapped,
5. Cognitively impaired

ii. Those with limited voluntariness who may be more likely to be affected by undue influence or coercion:

1. Prisoners,
2. Institutionalized individuals,
3. Individuals in hierarchical social/economic structures (i.e., employees, students, military personnel, family members of the research team)
4. Individuals in emergency situations
5. Individuals who are economically or educationally disadvantaged
6. Individuals who are marginalized in society, or
7. Individuals with fatal or incurable diseases

II. Scope

a. This policy and procedure applies to the following:

i. UTSW researchers, investigators and staff who are responsible for providing sufficient information concerning the inclusion of individuals with DADMC.

ii. The Human Research Protection Program Department (HRPPD) staff who are responsible for forwarding of the draft package for IRB review for pre-review submission documents for indications of DADMC populations.

iii. IRB members who are responsible for approving the inclusion of individuals with DADMC in research.

III. Procedures for Policy Implementation

a. Pre-review and Guidance

i. The PI identifies the categories of vulnerable subjects (e.g., cognitively-

impaired, children, prisoners, pregnant women, fetuses, employees, and students) involved in the research in the IRB application.

ii. The investigator answers specific questions in the IRB application which focus on ethical and regulatory issues pertaining to conduct of research involving the identified vulnerable population(s).

iii. Upon receipt of an IRB application, HRPPD staff conducts a preliminary screening. When applicable, HRPPD staff provides regulatory and educational materials to the IRB pertaining to DADMC populations as outlined in the 2.1. Initial Review Of Research, 2.2. Continuing Review Of Research, or 2.3 Modifications To Research policies. IRB members may also use the provided reviewer checklist, as a guide to conducting reviews.

iv. The HRPPD Staff, IRB Director (IRBD), IRB Chair, or designee requests a consultant review if additional expertise is needed. (See 2.1. Initial Review Of Research, 2.2. Continuing Review Of Research or 2.3 Modifications To Research).

v. IRB membership includes representation with expertise in selected vulnerable populations routinely reviewed by the IRB, such as children, pregnant women, and prisoners. HRPPD staff pre-review the application to ensure that designated representatives review research involving children or prisoners. Depending upon the type of review (convened IRB or expedited review), designated representatives may either attend the convened meeting or provide comments in writing.

b. IRB Review Process

i. The IRB shall consider whether including individuals with DADMC in the research is appropriate by considering the following:

1. The research should focus on an issue relevant to the DADMC population (should bear some direct relationship to the population's condition or circumstances). This population should not be chosen for

research that bears no relation to their situation just because it would be convenient for the researcher.

2. Appropriate inclusion/exclusion criteria. The IRB may require justification for any exclusion criteria that prohibits enrollment of a specific population.
3. Applicable or local laws that bear on the decision-making process (i.e., emancipated individuals, legally authorized representatives, age of majority for research consent).
4. Over-selection or exclusion of certain groups based on perceived limitations (i.e., targeting prisoners as research subjects because they are a readily available “captive” population).
5. If it is feasible to use another, non-DADMC population. The inclusion of a DADMC population is considered appropriate if the IRB determines that:
    a. the research could not be conducted without inclusion of the DADMC population, and
    b. there exist compelling reasons that mitigate any additional risk.

ii. The IRB should consider whether the research incorporates sufficient safeguards to ensure that the rights of the individual participants are protected, by considering the following circumstances.

1. Safeguards concerning mental capacity
    a. In research likely to involve persons with conditions or circumstances that are associated with possible diminished mental capacity and for those already determined to have DADMC (those with documented impaired decision-making capacity, incapacitated or legally incompetent), the IRB should determine whether the protocol has:

i. sufficient plans to assess mental capacity at time of enrollment and throughout study participation;

ii. Appropriate plans for obtaining consent from the subject or their legally authorized representative at time of enrollment and upon any changes in decision-making capacity; and

iii. whether additional protections should be included to protect this vulnerable population.

b. The assessment process should include acceptable physical and mental evaluation criteria at time intervals determined appropriate, given the specifics of the study.

c. In research likely to involve persons with diminished mental capacity, including those with impaired decision-making, incapacitated or incompetent, the IRB shall apply additional protections required under the applicable policy (e.g., state law)

2. Safeguards concerning voluntariness

a. Researchers should include plans to protect individuals with limited voluntariness. Examples of such individuals are:

i. Students/employees of the research team

ii. Family members of the research team

iii. Individuals in emergency situations or those with fatal or incurable diseases

iv. Individuals who are economically or educationally disadvantaged

b. For research which intends to involve persons who either have (at study entry) or are likely to develop diminished voluntariness (after study entry), the IRB application includes questions to assist the IRB with determining whether the plan to minimize coercion and

undue influence are appropriate. IRB considerations to determine appropriateness include:

i. Methods for identifying, recruiting and consenting the population

ii. Methods used to minimize undue influence during the research

iii. Study design. For example, it may be inappropriate to enroll a family member on a single-blind study

iv. Compensation.

c. The IRB should determine whether additional protections should be included to protect this vulnerable population.

d. Upon review, the IRB may determine that inclusion of the population is not appropriate.

iii. The IRB follows applicable federal and state regulations and IRB policy to review and approve proposed research that involves DADMC subjects such as:

1. Pregnant Women, Human Fetuses and Neonates (45 CFR 46, Subpart B)

a. For Non-DHHS funded research, the applicability of Subpart B is limited to research involving pregnant women as participants in research that is more than minimal risk and includes interventions or invasive procedures to the woman or the fetus or involving fetuses or neonates as participants.

2. Research Involving Prisoners (45 CFR 46, Subpart C) – Prisoner representatives review IRB applications involving prisoners and are present.

a. For Non-DHHS-supported research, the applicability of Subpart C is limited to the IRB's review and application of the additional protections for prisoners. Requirements related to certification or

approval by OHRP apply only to DHHS-supported research involving prisoners.

b. Participants who become prisoners after enrollment that was not previously reviewed, 45 CFR 46, Subpart C, the investigator must promptly notify the IRB.

   i. The IRB will determine whether the participant meets the definition of a prisoner and whether Subpart C applies.

   ii. Before terminating participation, the IRB will consider the risks of withdrawal to the participant's health, safety, rights, and welfare.

   iii. If continued participation is appropriate, the research must be reviewed under Subpart C.

   iv. If the participant cannot be withdrawn for health or safety reasons, the participant may remain enrolled while the IRB conducts its review.

   v. If Subpart C requirements cannot be fully met but continued participation is in the participant's best interests, the IRB may allow continued participation and notify OHRP of the determination and justification.

   vi. If continued participation is not appropriate, alternative mechanisms for continued access to the intervention, such as expanded access, compassionate use, or other clinical pathways, may be considered.

c. If a participant is temporarily incarcerated and the incarceration does not affect study participation or the applicability of Subpart C, the participant may remain enrolled.

   i. If the incarceration affects study participation or results in the

applicability of Subpart C, the IRB will follow the procedures above.

3. Research Involving Children (45 CFR 46, Subpart D, 21 CFR 50, Subpart D and U.S. Department of Education, Subpart D) – (See 3.1. Informed Consent Requirements).

    a. When research involves children who are wards of the state or another institution, and an advocate is required under applicable regulations, the IRB will require the appointment of an advocate for each child in addition to any individual acting on behalf of the child as guardian or in loco parentis. The advocate must have the background and experience necessary to act in, and agree to act in, the best interests of the child. The advocate must not be associated in any way, except in the role of advocate or IRB member, with the research, the investigators, or the child's guardian. The IRB will document its determination that the regulatory requirements for inclusion of wards are satisfied.

4. Research Involving Cognitively-Impaired Subjects – (the IRB application, and conformance with 3.1. Informed Consent Requirements and 3.2 Informed Consent By Surrogate);

iv. The IRB considers each of the specific findings discussed in the IRB application forms for research involving vulnerable subjects, as documented by IRB approval. IRB approval also documents that the IRB members acknowledge and agree with the description of safeguards and risk assessment of the protocol as described in the application by the PI. HRPPD staff document discussions of controverted issues at convened meetings in the IRB minutes (see 8.1 IRB Minutes).

v. HRPPD staff document specific findings in the meeting minutes, or expedited reviewers document determinations in accord with applicable

IRB/HRPPD policy. The IRB does not reapply the categories during subsequent reviews unless changes to the protocol dictate otherwise.

vi. The IRB may require more frequent review than once a year, for protocols involving vulnerable populations, based on the nature of the research and the level of risk.

IV. Definitions

See glossary of human research terms

V. References

a. 21 CFR 50: Protection Of Human Subjects

b. 45 CFR 46: Protection Of Human Subjects

c. 45 CFR 164: Security And Privacy (HIPAA Privacy Rule)

d. 21 CFR 56: Institutional Review Boards

VI. Revision and Review History

a. Revision Date: September 2026; Author: HRPP; Description: Clarified IRB responsibilities and safeguards for research involving individuals with diminished autonomous decision-making capacity, including added protections for prisoners, children who are wards, and requirements for applying Subpart C and related review considerations.

b. Revision Date: June 2021; Author: HRPP; Description: Separated policy from P&P manual. Updated references to AVPHRA and IRB Director. Minor administrative edits.

c. Revision Date: November 2019; Author: HRPP; Description: Limited voluntariness include family members of study team and expanded safeguard requirements

d. Revision Date: August 2017; Author: HRPP; Description: New Policy Development

e. Revision Date: March 2012; Author: IRB; Description: IRB Written Procedures