HRPP Policy Number: 1001 Version: 4.0 Effective Date: 08/15/25	Vulnerable Populations	Supersedes Document Dated: 12/01/16, 01/19/18, 01/21/19
Reviewed and Approved by: Tyler Ridgeway, Director, Research Integrity & Education	Reviewed and Approved by: Julia Dmitrieva, PhD, DU IRB Chair	

10.1 Inclusion of Vulnerable Populations in Research Activities

When some or all of the subjects who will be enrolled in a research study are likely to be vulnerable to coercion or undue influence, such as prisoners, children, individuals with impaired decision-making capacity, and economically or educationally disadvantaged persons, additional safeguards must be included in the study to protect the rights and welfare of these subjects.

In addition to the responsibilities prescribed for the IRB under 45 CFR Part 46, Subpart A, the IRB shall follow special procedures for prisoners, and children as specified in Subparts C and D. Inclusion of other vulnerable populations as research subjects is considered by the IRB and is discussed in further detail in this section.

10.2 Research Involving Prisoners

The IRB determines whether the criteria for approval of research are met when research involves prisoners.

Since prisoners (See **definition of prisoner and minimal risk in Section 2**) may be influenced by their incarceration to participate in research, and in order to assure that their decision to participate is not coerced, for research funded by HHS, the IRB will adhere to Subpart C of 45 CFR Part 46. Colorado Bureau of Prisons forms, if required, must be submitted directly to the appropriate agency for review and approval.

The University is considered "engaged" in research involving prisoners when an agent or employee of the University, for the purposes of the research obtains:

1. Data about the prisoner subjects through intervention or interaction with them; or
2. Identifiable private information about the prisoner subjects.
3. In addition, the University would become engaged in research involving prisoners if an agent or employee are the primary awardee of funds to conduct such research, even when all activities involving prisoner subjects are carried out by agents or employees of another institution.

10.2.1 IRB Review of Non-HHS Funded Research Involving Prisoners

For research that is not HHS-funded, the additional safeguards under 45 CFR 46.305(a)(2-7) will generally be followed, but the overall determination of whether or not to approve research for inclusion of prisoners (See **definition of prisoner in Section 2**) will be based on the criteria for approval specified in 45 CFR 46.111. Research will not have to meet one of the categories listed in 46 CFR 46.306. If an enrolled subject becomes incarcerated and the research was not initially approved for inclusion of prisoners, the following determination must be made:

1. The IRB Chair will determine whether it is in the best interests of the subject to remain in the study or to terminate enrollment and will decide whether it is feasible for the subject to remain in the study.
2. If it is determined that it is in the best interests of the subject to remain in the study, keep the subject in the study and review the research at the next convened IRB meeting with a prisoner advocate present.

When reviewing research that involves prisoners, the IRB will review and approve an appropriate consent process that includes a determination that:

1. The information will be presented in a language that is understandable to prisoners.
2. Each prisoner will be informed in advance that participation in the research will not affect his or her parole.

In addition, research requesting inclusion of prisoners as subjects may be reviewed by an expedited review process under the categories listed in **Sections 5.4.1** and **5.4.2**.

For research involving interaction with prisoners reviewed by expedited procedure:

1. Research involving interaction with prisoners may be reviewed by the expedited procedure if a determination is made that the research involves no greater than minimal risk for the prison population being studied.
2. Note: The prisoner representative must concur with the determination that the research involves no greater than minimal risk.
3. The prisoner representative must review the research as a reviewer, designated by the IRB Chair. This may be as the sole reviewer or in addition to another reviewer, as appropriate.
4. Review of modifications and continuing review must use the same procedure for initial review using this expedited procedure, including the responsibility of the prisoner representative.

For research that does not involve interaction with prisoners (e.g., existing data, record review), reviewed by expedited procedure:

1. Research that does not involve interaction with prisoners may be reviewed by the expedited procedure if a determination is made that the research involves no greater than minimal risk for the prison population being studied.
2. Review by the prisoner representative is not required.
3. The prisoner representative may review the research as a reviewer or consultant if designated by the IRB Chair.
4. Review of modifications must use the same procedures as the initial review.

10.2.2 IRB Review of HHS-Funded Research Involving Prisoners

Note: Studies involving prisoners will require approval of an authorized prison official. The IRB will require that copies of prison approval letters be uploaded with the IRB documentation.

For research funded by HHS, none of the exemption categories listed in **Sections 5.4.1** and **5.4.2** applies to research involving prisoners. In addition, even though it is not prohibited by 45 CFR Part 46, Subpart C, HHS-funded research requesting inclusion of prisoners as subjects will not be reviewed by an expedited review process. The IRB determines and documents that for DHHS research, all requirements for 45 CFR Part 46, Subpart C are followed. All such protocols will be reviewed at a convened meeting with a prisoner advocate present.

For HHS-funded research to include prisoners as subjects, a majority of the IRB members (exclusive of the prisoner advocate) must have no affiliation with the prison system, apart from membership on the IRB and at least one member who is a prisoner representative, with appropriate background and experience to serve in that capacity, must be present at any meeting at which protocols including prisoners will be discussed. In addition, the prisoner representative will be a voting member of the IRB, will be a primary or secondary reviewer, will receive all submitted protocol documents (initial review, modifications, continuing review), and will present their review at the IRB meeting. If no prisoner representative is present, review of proposals requesting inclusion of prisoners must be postponed, and no determinations on approval of protocols for inclusion of prisoners as research subjects may take place.

In addition to all other responsibilities prescribed under 45 CFR Part 46 Subpart A, the IRB shall review and approve HHS-funded research for inclusion of prisoners only if it finds the research under review represents one of the categories of research permissible in 45 CFR 46.306 (a)(2) (See **Section 12.3.3**) and meets all criteria under 45 CFR 46.305(a) as follows.

1. Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired.
2. The risks involved in the research are commensurate with the risks that would be accepted by non-prisoner volunteers.
3. Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator (PI) provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project.
4. The information is presented in language that is understandable to the subject population.
5. Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole.
6. Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examinations or care, taking into account the varying lengths of individual prisoner's sentences, and for informing participants of this fact.

10.2.3 Requirements by Categories in Research Involving Prisoners

45 CFR 46.306(a)(2)(A)

The study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects.

45 CFR 46.306(a)(2)(B)

The study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects.

46.306(a)(2)(C)

Research on conditions particularly affecting prisoners as a class (e.g., vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults), provided that the study may proceed only after the Secretary of HHS has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his/her intent to approve such research. Note: HHS Secretary consultation does not apply if research is not funded by HHS.

45CFR 46.306(a)(2)(D)

Research on practices, both innovative and accepted, that have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners, in a manner consistent with the protocols approved by the IRB, to control groups that may not benefit from the research, the study may proceed only after the Secretary of HHS has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his/her intent to approve such research.

Note: HHS Secretary consultation does not apply if research is not funded by HHS.

In accordance with the federal regulations, the IRB has the authority to waive the requirement that research activities fit Categories 1-4 listed above if the proposed research meets the following specific criteria:

a. The research involves epidemiologic studies in which the sole purposes are:
    i. To describe the prevalence or incidence of a disease by identifying all cases, or
    ii. To study potential risk factor associations for a disease, and
b. The IRB has determined that items in **Section 12.3.2** have been appropriately addressed and has also determined that:
    i. The research presents no more than minimal risk and no more than inconvenience to the prisoner-subjects, and
    ii. Prisoners are not a particular focus of the research.

10.2.4 Subjects that Become Incarcerated During HHS-Funded Research Study

If a subject becomes a prisoner while enrolled in a research study that was not reviewed according to the requirements in **Sections 12.3.2** and **12.3.3** above:

1. Confirm the subject meets the definition of a prisoner.
2. Terminate enrollment or review the research study under Subpart C if it is feasible for the subject to remain in the study.
3. Before terminating the enrollment of the incarcerated subject, the IRB should consider the risks associated with terminating participation in the study.
4. If the enrollment of the subject cannot be terminated for health and safety reasons:
    a. Keep the subject enrolled in the study and review the research under Subpart C.
    b. Note: If some of the requirements of Subpart C cannot be met, but it is in the best interests of the subject to remain in the study, keep the subject enrolled

and inform OHRP of the decision along with the justification.

c. Remove the subject from the study and keep the subject on the study intervention under an alternate mechanism such as compassionate use, off label use, etc.

10.2.5 Documentation and Certification of Research Involving Prisoners

Research activities that are approved for inclusion of prisoners as subjects must be documented in the IRB minutes that the research has been reviewed and meets the criteria for approval.

In addition, for research that is funded by the HHS, the IRB must also send a certification letter to the OHRP stating that:

1. The IRB has been constituted according to the regulations,
2. That the IRB has considered and made the seven findings set forth in 45 CFR 46.305, and
3. That the IRB finds that category A, B, C, and/or D of 46.306 permits the research to go forward with prisoners as human subjects. The certification letter should also provide a brief description of the research sufficient to allow OHRP to determine whether or not to concur with the IRB's findings or whether to consult with appropriate experts and publish a Federal Register notice. This requirement does not apply if not funded by HHS.

10.2.6 Colorado Department of Corrections (DOC) Approval

Investigators must obtain approval from the DOC Office of Planning and Analysis if research will be conducted within any Colorado corrections facility. Per Colorado Department of Corrections Administrative Regulation [2-C-1F-09] [4-4111], the DOC shall regulate the use and dissemination of research findings. All research projects and subsequent dissemination of research findings shall be reviewed by the manager of Planning and Analysis. This procedure shall apply to outside research requests, internal research proposals, conference presentations, professional journal submissions, and book proposals concerning DOC operations, services, and correctional programs.

1. All surveys requesting any information about the DOC and/or information about offenders shall be routed through the Office of Planning and Analysis. This includes surveys sent by federal agencies, private companies, colleges and universities, individuals, DOC employees, contract workers, volunteers, and non-profit organizations (e.g., victim advocates).
2. Any research proposal must first be reviewed and approved by the Office of Planning and Analysis. A detailed research proposal shall be submitted to the Office of Planning and Analysis in accordance with AR Form 1400-03A, Research Request Form. The Research Advisory Panel shall convene at least once per month to review proposals.
3. A written response to acknowledge receipt of the research request will be made to the applicant within three working days of receipt of the written request.
4. Any research proposal and associated research design must first be reviewed by the Research Advisory Panel, in consultation with the manager of the Office of Planning and Analysis. The manager of the Office of Planning and Analysis will forward the proposal and recommendation to the executive team for review. The executive team, in consultation with the administrative head(s), shall return its decision to the manager of the Office of Planning and Analysis.
5. The manager of the Office of Planning and Analysis will notify the principal investigator of acceptance or denial. Proposals that are approved will be assigned a research liaison from the Office of Planning and Analysis.
6. A letter of agreement to conduct research must be signed by the principal investigator and the manager of the Office of Planning and Analysis.
7. The University of Denver Institutional Review Board approval is required for all Colorado DOC projects, such as projects receiving federal funding, involving

university personnel or students, involving direct contact with offenders, or requiring confidential or personal data.

10.3 Research Involving Children

Note: Studies involving children in schools will require approval of the school district(s) and parental permission. So as not to unnecessarily delay review and approval of a study, IRB applications and requests for district permission to conduct the study should, when allowed by the school district(s), be submitted simultaneously. The IRB will require that copies of district approval letters be uploaded with the IRB documentation.

10.3.1 IRB Review of HHS-Funded Research Involving Children

In reviewing HHS-funded research requesting the inclusion of children as research subjects, it is necessary to apply special safeguards as prescribed in 45 CFR 46, Subpart D in addition to the responsibilities prescribed in other Subpart A. Special risk/benefit determinations must be discussed and documented by the IRB in the minutes as to the specific paragraph and subparagraph(s) under which the research is approved.

In addition, some funding agencies may have additional IRB membership requirements. For example, the National Institute on Disability and Rehabilitation Research (NIDRR) specifies that when an IRB reviews a NIDRR-funded research project that purposefully includes children with disabilities as research subjects, the IRB must include at least one person whose primary interest is the welfare of children with disabilities. When reviewing these types of research projects, the IRB will use ad hoc reviewers (consultants) with specific expertise in treating children with disabilities.

10.3.2 Requirements by Category in Research Involving Children

Research involving Children as subjects must meet one of the following categories:

1. **45 CFR 46.404** -Minimal Risk with or without a potential for direct benefit.
    a. Adequate provisions need to be made for obtaining assent of the children.
    b. Adequate provisions must be made to obtain permission of parents or guardians (Permission Form).

2. 45 CFR 46.405 - Greater than Minimal Risk with a potential for direct benefit (to each individual subject).
    a. IRB must find that the risk is justified by the anticipated benefits.
    b. The relation of the anticipated benefit to risk is at least as favorable as alternative approaches.
    c. Adequate provisions must be made for obtaining assent of the children.
    d. Adequate provisions must be made to obtain permission of parents or guardians (Permission Form).

2. **45 CFR 406** - Greater than Minimal Risks with no prospect of direct benefit, but likely to provide generalizable knowledge about the subject's disorder or condition and:
    a. The risk represents a minor increase over minimal risk.
    b. The intervention or procedure presents experiences commensurate with those inherent in the subjects' actual or expected medical, dental, psychological, social, or educational experience.
    c. The intervention or procedure yields generalizable knowledge about the subjects' disorder or condition that is vital to understanding or ameliorating the subjects' disorder or condition.
    d. Adequate provisions must be made for obtaining assent of the children.
    e. Adequate provisions must be made to obtain permission of parents or guardians (Permission Form).
3. **45 CFR 46.407** - Greater than Minimal Risks with no prospect of direct benefit and

cannot meet the conditions specified in the category of 45 CFR 406 (Number 3 above a-e). The research is not otherwise locally approvable but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. Research in this category must meet the following requirements:

a. The IRB must find that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health and welfare of children.
b. A request must be made by the PI, through the IRB, to the Secretary of HHS or the Commissioner of FDA to approve the research. The Secretary or Commissioner, after consultation with a panel of experts in pertinent disciplines and following opportunity for public comment, may approve the research.

Research that involves children and is not HHS-funded must meet one of the approvable categories described in **Section 12.4.2 (1-3)**. However, for research falling under category 45 CFR 46.407 (See **Section 12.4.2 (4)**) and not FDA regulated, the PI must request that the IRB establish an expert panel to review the research. Based on the recommendations of the panel, the IRB will consider the research for approval.

10.3.4 Assent/Permission Requirements for Research Involving Children

Requirements for documentation of assent depend on the age, maturity, and psychological state of the child:

1. For children under the age of 7, assent is waived or verbal assent is obtained as determined by the IRB.
2. For children ages 7-12, a simple assent form is used and verbal assent is obtained. The child does not have to sign the assent form.
3. For children ages 13-17, a simple assent form is used, verbal assent is obtained, and the child must sign the assent form.
4. If the research is approvable under 45 CFR **46.404 46.405**, **only one parent's signature is required.**
5. If the research is approvable under 45 CFR **46.406, 46.407**, **both parents must sign the parental permission form, unless one parent is unavailable or not competent to consent.**
6. For research approved under 45 CFR 46.404, 46.405, the parents can override a child's decision not to participate. Parents cannot override a child's decision not to participate if the research is approvable under 45 CFR 46.406, 46.407. The IRB could waive the requirement for the child's assent, in which case the parents could override the child's decision to participate for all research activities.
7. A legal guardian could only give permission for inclusion of a child as a research subject if the document granting guardianship authorizes the person to give permission for "medical care, including research."

10.3.5 Exceptions to Assent Requirements for Research Involving Children

When the IRB determines that assent is not a requirement for some or all children in a study, the IRB determines and documents one or more of the following:

1. The children are not capable of providing assent based on their age, maturity or psychological state.
2. The intervention or procedure holds the prospect of direct benefit that is important to the health or well-being of the child and is available only within the context of the research, and the capability of the children is so limited that they cannot reasonably be consulted.
3. Assent can be waived using the criteria for waiver of the consent process.

10.3.6 Waiver of Permission Requirements for Research Involving Children

Generally, written documentation of parental permission is required when recruiting and enrolling subjects who are children. The documentation must signify "active" permission in which the parent specifically signs the document granting permission for the child to

participate in the research. “Passive” permission, in which the researcher assumes that if the permission form is not returned, the parent has granted implied permission, is not allowable.

However, the IRB will consider requests for a waiver of the requirement for parental permission and/or a waiver of the requirement to obtain written documentation of consent on a case-by-case basis, determine if a waiver is appropriate and/or permissible under 45 CFR 46.408(c), and document its findings and determination. The IRB may determine that the research protocol is designed for conditions or for a subject population for which parental permission is not a reasonable requirement to protect the subjects and may approve a waiver, provided that an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted and the waiver is consistent with federal, state, and local law.

If the research will be conducted in a school setting, a waiver of the requirement for parental permission and/or the requirement for written documentation of parental permission may not be allowable under the requirements of the **Protection of Pupil Rights Amendment**.

10.3.7 Reimbursements to Children and/or Parents

For many studies, especially those conducted in schools, reimbursement is generally not appropriate. However, if a researcher believes that reimbursement is appropriate, the following general guidelines, as described in **Section 4.8**, should be adhered to:

1. Any compensation should not be contingent upon the subject completing the study, but should accrue as the study progresses.
2. Unless it creates undue inconvenience or a coercive practice, compensation to subjects who withdraw from the study should be made at the time they would have completed the study, had they not withdrawn.
3. Compensation given as a “bonus” or incentive for completing the study is technically acceptable to the FDA, provided that the amount is not coercive. However, this sort of compensation is usually viewed by the IRB as coercive. The IRB is responsible for determining if the amount is not so large as to be coercive or represent undue influence.
4. The amount of compensation should be clearly set forth in the assent and parental permission forms.

When considering the amount of reimbursement to be given to a child and/or the child’s parents, special consideration must be given to ensure that the child does not simply assent to participate based on the amount or type of reimbursement. In addition, the amount of reimbursement should not be so large that the parents would provide undue pressure on the child to assent to participate. The PI should consider that the type or amount of reimbursement may be coercive in some situations and not coercive in others, and make every effort to establish a reimbursement amount and schedule that will not be a factor in the child’s decision whether to participate or the parent’s decision to give permission for a child’s participation.

10.3.8 When a Child Reaches the Age of Consent While Enrolled in a Study

Informed consent should be viewed as an ongoing process throughout the duration of a research project. When a child who was enrolled in research with parental or guardian permission subsequently reaches the legal age of consent (18 years old in Colorado) to the procedures involved in ongoing research, the subject’s participation in the research is no longer regulated by the requirements of 45 CFR Part 46, Subpart D regarding parental or guardian permission and subject assent.

Unless the IRB determines that the requirements for obtaining informed consent can be waived, the PIs should seek and obtain legally effective informed consent as described in

Section 6 for the now-adult subject for any ongoing interactions or interventions with the subject. This is because the prior parental permission and child assent are not equivalent to legally effective informed consent for the now-adult subject. However, the IRB could approve a waiver of informed consent if it finds and documents that the criteria for waiver are met.

Similarly, if the research does not involve any ongoing interactions or interventions with the subjects, but continues to meet the regulatory definition of "human subjects research" (e.g., continued analysis of specimens or data for which the subject's identity is readily available to the PI), it would be necessary for the PI(s) to seek and obtain legally effective informed consent of the now-adult subjects. The IRB may consider, if appropriate, a waiver of the requirements for obtaining informed consent in order for the subjects to continue to participate in the research.

10.3.9 Wards

Children who are wards of the state or any other agency, institution, or entity can be included in research approved under 45 CFR 46.406 or 45 CFR 46.407 only if such research is:

1. Related to their status as wards; or
2. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children as subjects are not wards.

Research approved for inclusion of wards under 45 CFR 46.406 or 45 CFR 46.407 shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as a guardian or *in loco parentis*. One individual may serve as an advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the PI(s), or the guardian organization.

10.4 Other Vulnerable Populations

Although there are no specific regulations governing the inclusion of other groups of vulnerable persons in research, there are other vulnerable populations that may be approached for enrollment in research protocols. A vulnerable population is one in which there is potential for real or perceived coercion or undue influence for subjects to enroll in the study, or the subjects may be incapable of fully understanding the potential risks of the research. In all cases, the IRB must consider the possibility and justification for including these subjects in the proposed research and safeguards to protect their rights and welfare.

10.4.1 Research Involving Individuals with Impaired Decision-Making Capacity

Special procedures for IRB review and approval apply to research activities involving potential research subjects who, for a wide variety of reasons, are incapacitated to the extent that their decision-making capabilities are diminished or absent. Impaired capacity is not limited to individuals with neurologic, psychiatric, or substance abuse problems. Conversely, individuals with these problems should not be presumed to be cognitively impaired.

The following guidelines are taken from a document produced by the OHRP as "Points to Consider". The OHRP intends that these points be considered by IRBs and PIs in their effort to protect research subjects.

Initially, the PI must assess whether or not the study could be performed utilizing competent subjects (those without impaired decision-making capacity) and determine that competent persons are not suitable for the proposed research. PIs must demonstrate to the IRB that there is a compelling reason to include incompetent individuals or persons

with impaired decision-making capacity as subjects by considering the following:

1. Incompetent persons or persons with impaired decision making capacity are not being proposed as subjects simply because they were readily available;
2. The proposed research entails no significant risks, tangible or intangible, or if the research presents some probability of harm, there is at least a greater probability of direct benefit to the subject;
3. The research does not impose a risk of injury, unless the research is intended to benefit each subject and the probability of benefit is greater than the probability of harm;
4. Procedures are devised to ensure that subjects' legally authorized representative (LAR) are well informed regarding their roles and obligations to protect incompetent subjects or persons with impaired decision-making capacity;
5. LARs will be told that their obligation is to try to determine what the prospective subject would do if competent, or if the prospective subject's wishes cannot be determined, what they think is in the incompetent person's best interest.

Potential or actual research subjects who may have impaired decision-making capacity may not understand the difference between research and treatment or the PI's role as both clinician and PI. Therefore, it is essential that the consent process clearly indicate the differences between individualized treatment and research and between the roles of clinician and PI. Mental or decisional impairment may include, but is not necessarily limited to, psychiatric disorders, organic impairments, developmental disorders, persons under the influence of drugs or alcohol, persons with traumatic injuries, and women in labor.

The following is a list of general guidelines to be considered:

1. Each IRB includes at least one voting member, independent of the research and with appropriate professional background, knowledge, and experience in working with individuals with questionable decision-making capacity. The IRB will also consider including additional voting members from the community, perhaps representatives of patient advocacy groups.
2. PIs should be sensitive to differing levels of capacity and use assessment methods tailored to the specific situation. Also important is the PI's timing of the assessment in order to avoid periods of heightened vulnerability. Both the IRB and PIs must recognize that decision-making capacity may fluctuate and require ongoing assessment throughout the course of the research.
3. Responsibilities of the IRB are significant and will reflect heightened vigilance in reviewing protocols proposing to include this vulnerable population. As such, not all projects proposing to include decisionally-impaired persons should or will be approved by the IRB.
4. As the level of impairment increases, along with an increase in risks and discomforts, safeguards should also increase proportionate to the severity of the impairment. Provisions for additional safeguards should be in place prior to involving subjects in more than minimal risk research when the subjects' decision-making capacity is impaired. PIs should provide ongoing efforts to enhance the subjects' understanding and appreciation of their role in the research.
5. IRBs and PIs should be creative in choosing appropriate protections. Other options that may be used to provide additional protections may include:
    a. Use of an independent monitor to assess the potential subject's decision-making capacity or to be present during subject recruitment and the consent process. If the impairment in decision-making capacity is based on a diagnosis of mental illness, the PI should obtain consultation with a psychiatrist or licensed psychologist.
    b. Use of a family member or other LAR as a surrogate for research decisions. This must be approved by the IRB and should be documented on the consent form. The representative should be authorized to give permission for

"medical care including research."

6. The autonomy of the individual with impaired decision-making capacity should be respected. Their assent to participate in the research should be obtained, whenever possible, and their decision to withdraw from a study at any time should be honored.
7. Use of an advance directive for research may be considered.
8. Since informed consent is an ongoing process throughout the course of the research, a written summary of important information about the research may be useful when provided on a regular basis. Communication between PIs and their staff and the participants and their families is critical.
9. Individuals with impaired decision-making capacity may need more time to consider the information they are given regarding the research. Information should be provided incrementally to facilitate understanding. Planned waiting periods to allow potential participants to consult with family members about whether to participate or not may be useful.
10. IRBs and PIs must strive for a balance that maximizes potential benefits, recognizes individual autonomy, and minimizes risks associated with the research.

10.4.2 Economically or Educationally Disadvantaged Persons

According to the Federal regulations at 45 CFR 46.111(a)(3) and .111(b), when some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as the educationally or economically disadvantaged, additional safeguards must be included in the study to protect the rights and welfare of these subjects. The IRB will review protocols that are likely to include educationally/economically disadvantaged subjects for special risks that may be present for this group, i.e., the potential for undue influence/coercion in recruitment or enrollment, the potential for enrolling more subjects from this group than from other groups because of their vulnerability, etc.

Dated 01/21/19, per revised Common Rule, description of "vulnerable" was revised, removed "pregnant women' as vulnerable population, replaced "handicapped or mentally disabled persons" with "individuals with impaired decision-making capacity, and added "economically or educationally disadvantaged persons". Colorado Department of Corrections (DOC) was integrated into HRPP policy