1 PURPOSE

1.1. The purpose of this guidance is to assist researchers in complying with the applicable policies and procedures in the performance of research involving vulnerable populations not otherwise covered under 45 CFR 46 Subparts B, C, or D.

1.2. This document includes guidance on research involving economically or educationally disadvantaged persons, persons with impaired decision-making capacity, limited or non-English speakers, and students or employees of an organization.

2 BACKGROUND

2.1. "Economically or educationally disadvantaged" means:

2.1.1. Persons placed at special risk by socioeconomic and educational background.

2.1.1.1. Economically disadvantaged persons include those persons who struggle to provide basic necessities for themselves and their families or communities.

2.1.1.2. Educationally disadvantaged persons may have educational deficits, learning disabilities, or cultural backgrounds that limit communication with a researcher.

2.2. "Impaired Decision-Making Capacity" means:

2.2.1. Persons having a psychiatric or developmental disorder that affects cognitive or emotional functions to the extent that the capacity for judgment and reason is significantly diminished.

2.2.2. Persons, including those under the influence of or dependent on alcohol or drugs, those affected by degenerative brain diseases, those who are terminally ill, and those who have severe physically disabling handicaps, may be compromised in their ability to make decisions in their best interests.

2.3. "Vulnerable Population" means:

2.3.1. Persons vulnerable to coercion or undue influence.

2.4. Investigator guidance for research involving vulnerable populations covered by Subparts B, C, or D of 45 CFR 46 are as follows:

2.4.1. 405 Investigator Guidance- Research Involving Pregnant Women, Fetuses, and Neonates

2.4.2. 406 Investigator Guidance- Research Involving Prisoners

2.4.3. 407 Investigator Guidance- Research Involving Children

2.4.4. 408 Investigator Guidance- Classroom Research

2.4.5. 413 Investigator Guidance- Additional Department of Education Obligations

3 GUIDANCE

3.1. *Economically disadvantaged* persons may be at risk for undue influence through compensation, or real or perceived threats to their economic standing such as job loss; educationally disadvantaged persons may be at risk for undue influence through comprehension of research materials or activities, or through language barriers.

3.1.1. Subjects may have limited health literacy and numeracy so consent documents must be written in language that is easily understandable and appropriate for the population.

3.1.2. Study staff must assess understanding and facilitate an ongoing dialogue.

3.1.3. The possibility of illiteracy or limited reading ability must be accounted for and plans to address this put in place for both the consent document and consent process.

3.1.4. Compensation cannot be coercive or unduly influence subjects. The IRB will review proposed subject compensation on a protocol-by-protocol basis including the type of compensation and amount, schedule, and pro-ration of payments to assure that the proposed compensation is not so significant that prospective subjects may consider participation in research that they may otherwise not participate in if it were not for the compensation.

3.1.5. The proposed method and timing of disbursement should not present undue influence.

3.1.6. Recruitment materials may not promise "free" treatment or emphasize the medical care that participants may receive during the research.

3.1.7. To ensure equity in enrollment, other factors bear consideration when planning research for persons who are economically disadvantaged (e.g., costs for childcare or transportation).

3.1.8. Safeguards must be in place during the consent process and throughout the research relationship to ensure open and free communication between the researcher and the prospective participant.

3.1.9. Because influence is contextual, and undue influence depends on the individual situation, the investigator should evaluate potential during the consent process.

3.1.10. Benefits should be appropriate for the risks involved and should not cause inequitable subject selection and must be considered fair for all individuals involved.

3.1.11. Receipt of treatment/placebo should be provided in equal opportunities across socioeconomic statuses.

3.2. Scientifically and ethically appropriate research involving individuals *with impaired decision-making capacity*, such as those under the influence of substances like alcohol or drugs, those with psychiatric disorders (e.g., psychosis), developmental disorders (e.g., intellectual disability), and organic impairments (e.g., stroke, dementia) is critical to illuminate the underlying mechanisms that lead to these conditions and to identify promising treatments.

3.2.1. Individuals with impaired decision-making capacity may be enrolled in research only when their participation in the study is justified, capacity to consent is assessed and documented, and provisions for surrogate permission are in place (for participants who are incompetent).

3.2.2. Researchers and the IRB must consider the degree to which these conditions may impair an individual's capacity to consent to participation in research, including when decisional capacity may fluctuate over time and plan the research accordingly.

3.2.3. Investigators planning research in which adults with impaired decision-making capacity will be enrolled must provide the IRB with the following:

3.2.3.1. Scientific justification for involving this population in the research;
3.2.3.2. Plan for assessing capacity to consent or assent;
3.2.3.3. Plan for obtaining surrogate consent, as necessary; **and**
3.2.3.4. A description of the procedures that are designed to minimize risks to participants.

3.2.4. The capacity to consent of individuals with impaired decision-making capacity may be unknown. Researchers should not assume that a prospective participant is unable to provide consent. Rather, researchers should seek to objectively determine whether a prospective participant can provide informed consent. PIs must ensure that the research team members responsible for assessing capacity to consent have the expertise necessary to accurately evaluate each prospective participant's ability to:

3.2.4.1. Act on their own behalf.
3.2.4.2. Comprehend the information presented, including study purpose and procedures.

3.2.4.3. Understand the risks and benefits of the research as it related to their own health condition.
3.2.4.4. The alternatives to participation.
3.2.4.5. Provide clear and effective consent or assent.

3.3. Research involving *persons with limited or non-English speaking individuals* is important to ensure the benefits of research are justly distributed and to address research topics that are specific to such populations. Regardless of the reasons for involving individuals with minimal or no English-language skills in research, researchers must design recruitment and consent processes to ensure prospective participants comprehend what is being asked of them and voluntarily agree to participate.

3.3.1. A limited or non-English speaker is any person who, by reason of place of births or culture, speaks a language other than English and does not speak English with adequate ability to communicate.
3.3.2. Researchers should be aware that there are cultural concerns and appropriateness for language that may need to be addressed. For example, certain words or phrases may not translate well (or at all) in each language.
3.3.3. Federal regulations (45CFR46.116; 21CFR50.20) require consent documents to be in language understandable to the participant.

3.3.3.1. For research posing greater than minimal risk, researchers must obtain legally effective signed consent from each participant in accordance with DHHS requirements for informed consent (at 45 CFR 46.116) and for documentation of informed consent (at §46.117), which includes use of a short form written consent document.
3.3.3.2. For minimal risk research, researchers may use simplified information scripts/sheets and oral consent in lieu of a consent form, including a short form consent document. NOTE: For minimal risk research that is conducted or supported by federal funds, or that involves prisoners or incomplete disclosure/deception, the IRB must approve an alteration of informed consent (at §46.116(2)) and a waiver of the requirement to obtain a signed consent form (at §46.117(c)(1) or (2)).

3.3.4. Ideally, the research team will include individuals fluent in the language spoken by prospective participants. If researchers and participants are not fluent in the same language, interpreters are needed for recruitment and consent, and for interviews, focus groups, or other verbal interactions with participants. Interpreters must:

3.3.4.1. Have sufficient knowledge about the research to correctly respond to questions from prospective participants;
3.3.4.2. Demonstrate a basic understanding of the importance of voluntary participation; **and**
3.3.4.3. Agree to limit their comments to the information provided in the IRB-approved consent materials.
3.3.4.4. Be willing to respect the privacy of individual participants and maintain the confidentiality of the information provided by the participant.

3.3.5. Investigators must consider the relationship of the interpreter to the interviewee and to the community.

3.4. *When a study population includes students*, who receive instruction directly from one or more researchers, recruitment strategies must be designed to ensure voluntary participation. Students' decisions about research participation may not affect (favorably or unfavorably) grades, letters of recommendation, or other opportunities or decisions made by teacher/professor-researchers.

3.4.1. Instructors cannot mandate or require student participation and care should be taken to eliminate or reduce the risk that they may unduly influence or coerce student participation in research.

3.4.2. Alternative assignments must be provided to students who decline participation, when research activities involve instruction or extra credit.

3.4.3. If the instructor is also the researcher, they should arrange to have consent and/or data collected via independent third party.

3.4.3.1. A teaching assistant for a class in which the student is enrolled does not qualify as a third party.

3.4.4. Whenever possible, researchers should avoid data collection during regular class meetings.

3.4.4.1. For researchers using pre- and post- tests to determine the efficacy of a particular curriculum, a third party should obtain the consent forms and distribute the tests when the researcher is not present.

3.4.5. If the research is one where data are collected from a group project or audio- or videotape of the group interaction, each student's consent is necessary for the use of that data in the research. If one student does not consent, the data may be used only if the non-consenting student's data can be effectively excluded. Special data storage considerations should be given to protecting the confidentiality of video and audio research data, including encryption measures and secure, locked physical storage locations.

3.4.6. Regardless of the student age or level of enrollment, research that includes access to student records must adhere to the Family Educational Rights and Privacy Act (FERPA) and when funded by the Department of Education, the Protection of Pupil Rights Amendment (PPRA). *Reference "Investigator Guidance: Additional ED Obligations (HRP-410)" for more information on FERPA and PPRA*.

3.5. Recruitment of *potential participants who are employees* under supervisions on a member of the research team must be designed to minimize the possibility of coercion or undue influence. In general, potential participants should be solicited from a "broad base" of individuals meeting the conditions for study, rather than from individuals who report directly to the investigator(s).

3.5.1. Strategies to minimize the potential influence of an investigator when recruiting their own employees include recruitment through a third party unassociated in a supervisory relationship with the employee, postings or sign-up sheets, or other methods that require an employee interested in participation to initiate contact with the investigator(s).

3.5.2. An employee's decision about research participation may not affect (favorably or unfavorably) performance evaluations, career advancement, or other employment-related decisions made by peers or supervisors.

3.5.3. Additional safeguards may be needed to protect the privacy interests of employees who are also research participants. Workplace conditions may make it difficult for investigators to keep an individual's participation confidential, which could pose risks to participants, e.g., when stigma is associated with the condition or question under study or when peer pressure is a component of the research. In such situations, research should be conducted off-site and/or outside of regular work hours when possible to minimize potential risks.

3.5.4. In cases where regular workplace activities are also the topic of research, investigators must clarify for potential research participants those activities that are optional and distinct from any mandatory workplace activities that would take place even without the research. When access to individuals or the facilities of the site is needed for recruitment and/or research activities, a letter of support from someone authorized to speak on behalf of the employees/site may be required.

4 REFERENCES

4.1. 45 CFR 46.116
4.2. 45 CFR 46 Subpart B
4.3. 45 CFR 46 Subpart D
4.4. 21 CFR 50.20
4.5. 21 CFR 50 Subpart B
4.6. 21 CFR 50 Subpart D