Guidance: Assessing Research Risks
Approval Criteria #1 & 2

Overview

Approval criteria #1: **Risks to subjects are minimized.**

Approval criteria #2: **Risks to subjects are reasonable in relation to benefits.**

Risk in human subject research is the probability of harm or injury (physical, psychological, social, legal, or economic) occurring because of participation in a research study. Both the probability and magnitude (severity) of a possible harm may vary from minimal to significant. The magnitude of potential harm is the summative measure of its severity, duration, and reversibility. Thus, a research protocol with a low probability of harm occurring, but a high severity of harm if it occurs, may be determined to be greater than minimal risk (e.g. a severe allergic reaction to a new medication, or stigmatization from unintentionally releasing HIV status of participants). Alternatively, a protocol with a high probability of harm occurring, but a low severity of harm, may be assigned minimal risk for participants (e.g. itchiness after electrode tape removal, or distress related to answering sensitive, personal questions).

This guidance details types of research risks and strategies that may minimize the possibility of these risks.

Definitions

Benefit: A helpful or good effect, something intended to help, promote or enhance well-being; an advantage.

Risk: The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant.

Minimal Risk means 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.

Privacy: an individual's desire to control access of what is shared about themselves with others.

Confidentiality: refers to the researcher's agreement with the participant about how the participant's identifiable private information will be handled, managed, and disseminated.

Types of risks to research participants

Physical Harms: pain, discomfort, or injury from a procedure or side effects from a drug. The physical harm could be permanent, but most are transient, e.g., nausea, dizziness, headaches, muscle soreness, numbness, and tingling.

Psychological Harms: undesired changes in thought processes and emotion, e.g., episodes of depression, confusion, feelings of stress, guilt, loss of self-esteem, embarrassment, and distress. The possibility of psychological harm may be more prevalent when the research involves an element of deception.

Invasion of Privacy: One's perception/observation of behavior that is considered private.

Loss of Confidentiality: the risk of breach of confidentiality concerns safeguarding information given voluntarily by one person to another.

Social Harms: may result in embarrassment within one's business or social group, loss of employment, or criminal prosecution.

Economic Harms: any costs accrued from participating in a study.

Legal Harms: an interaction between the participant and the court system.

Role of the investigator

Researchers should provide detailed information in the IRB protocol about potential risks and benefits associated with the research and provide information about the probability, magnitude, and potential harms associated with each risk. Please keep in mind that these risks are to be directly related to participation in the research components themselves and be immediate or reasonably foreseeable risks. They should not be risks or benefits of procedures or interventions individuals would receive even if not participating in the study and they should not be long-range effects of applying knowledge gained in the research.

Strategies to minimize risk

Risks, even when unavoidable, can be reduced or managed. Precautions, safeguards, and alternatives can be incorporated into the research activity to reduce the probability of harm or limit its severity or duration. An important aspect of risk assessment is the nature and type of planned protections to minimize the probability and/or severity of potential harm to participants. A greater than minimal risk may be reduced to minimal risk if protections for

research participants are judged to be adequate. For example, a breach of confidentiality of sensitive information poses a risk of serious harm, but protections such as restricted access (encrypted data storage, locked files, Certificates of Confidentiality) reduce the absolute risk significantly and may thereby render a minimal overall risk to participants.

To minimize risk to study participants, consider the following:

- Use procedures that are consistent with sound research design and that do not unnecessarily expose participants to risk.
- Provide complete information in the protocol regarding the experimental design and the scientific rationale underlying the proposed research, including the results of previous research.
- Assemble a research team with sufficient expertise and experience to conduct the research.
- Ensure that the projected sample size is sufficient to yield useful results.
- Develop inclusion/exclusion criteria that will enroll only the desired population of interest.
- Collect data from standard-of-care or methodologically appropriate procedures to avoid unnecessary risk, particularly for invasive or risky procedures.
- For studies involving an element of deception, provide a thorough debriefing following completion of the study.
- Provide up-to-date resources for additional help/support for participants (counselors, rehab centers, etc.).
- Incorporate adequate safeguards into the research design such as an appropriate data and safety monitoring plan and the presence of trained personnel who can respond to emergencies.
- Store data in such a way that it is impossible to connect research data directly to the individuals from whom or about the data pertain; limit access to key codes and store separately from the data.

Role of the IRB

The IRB is responsible for evaluating the potential risks and weighing the probability of the risk occurring and the magnitude of harm that may result. It must then judge whether the anticipated benefit, either of new knowledge or improved health for the research subjects, justifies asking any person to undertake the risks

In evaluating risks and benefits, the IRB will consider only those risks and benefits that are directly related to participation in the research, as distinguished from risks and benefits of procedures/interventions individuals would receive even if not participating in the research.

IRB considerations include:

- identifying the risks associated with the research, as distinguished from the risks of therapies the subjects would receive even if not participating in research;
- determining that the risks will be minimized to the extent possible;
- identifying the probable benefits to be derived from the research;
- determining that the risks are reasonable with benefits to subjects,
- ensuring that potential subjects will be provided with an accurate and fair description of the risks or discomforts and the anticipated benefits.

Examples of applying strategies to minimize risk

Loss of Time: Researchers are required to include the estimated time of each study activity and the total time of completion on the informed consent (parent permission or assent form). Researchers should:

- Estimate study completion time based on pilot tests.
- Consider the reading level of participants (e.g., 3rd-grade readers vs. post-secondary students) when calculating the time necessary to complete the study.
- Reasonably overestimate times to account for participants that may take longer.
- Prepare for potential time delays when using online software (e.g., Zoom) or introducing new activities.

Traumatic Events: Recalling traumatic or distressing events can be uncomfortable, and in some cases, harmful to an individual. While it is not always possible to identify what types of questions may trigger participants, researchers should identify and disclose questions or activities about traumatic events. Researchers should:

- Disclose any topics, study activities, or questions triggering in the informed consent. For example, if the study includes questions about a traumatic event (e.g., 9/11), provide a trigger warning such as "The next section will include questions that may be uncomfortable to you. This study is voluntary. You can choose to stop the study at any time or skip any question."
- Monitor the participant during each study activity and after, if possible. While the participant may appear fine during a study, recalling traumatic events may lead to flashbacks, insomnia, trouble concentrating, or higher levels of anxiety, sadness, or anger for a prolonged period of time.
- Provide participants with a list of community resources, or offer free counseling services (if appropriate), should the need arise.
- Consider options such as recruiting a trained professional to be available to help debrief the participants if they start to experience symptoms of distress.

Unwanted Stimuli: Exposure to unwanted or distressing stimuli during a study's activities may bring harm and discomfort. Participants should not be exposed to distressing stimuli, e.g., pornography, smoking, suicide, without first providing their clear consent. Researchers should:

- Know the risks associated with exposing participants to unwanted stimuli (e.g., increased sadness or irritability), and implement additional safeguards throughout their study, such as debriefing participants after the study activities are finished.
- Refrain from exposing high-risk groups to unwanted stimuli. For example, study activities including heavy drinking or intoxication should screen out recovering substance users.

Environmental Stimuli: Environmental stimuli, such as the research location, building layout, lighting, or external noise, are not always considered in the research design. However, some stimuli may be triggering for participants and should be eliminated, if possible. Researchers should:

- Examine their research space for any environmental allergens or health issues, such as dust and flickering lights, before inviting participants.
- Remain mindful of possible food allergies (e.g., nuts, shellfish, gluten) when serving snacks or refreshments.
- Ensure that the space is safe, secure, hygienic, and, if applicable, private.
- Review the CDC's detailed instructions on how to clean and disinfect workspaces, along with their list of EPA-approved disinfectants.

Minor Emotional Risk: Typical common, but minor, risks include mental fatigue, embarrassment, discomfort, or frustration. Researchers should:

- Review their study activities from the perspective of the participant to determine if these emotions might be encountered.
- Always disclose any anticipated distressing emotions in the consent form.

Exercise & Repetitive Movements: Studies involving exercise or movement have an inherent risk of physical injury to the participants. Researchers should:

- Disclose all activities at the beginning of the study that may cause physical discomfort.
- Evaluate or discuss the participants' physical health and ability based on the study activity.
- Consult with the
- Disclose health risks on the consent form.

Personal Information: Asking questions about private information such as income, health habits, illegal substance use, etc. may be distressing for participants. Inclusion of these types of questions should be clearly justified to the IRB. Researchers should:

- Clarify confidentiality policies.
- Disclose what identifiers may be disclosed, or are at risk of disclosure (e.g., during focus group sessions, researchers cannot guarantee confidentiality).

Resources

- **Common Rule, 45 CFR Part 46**
- Columbia University
- NIH, Coping with traumatic events
- University of California, Davis
- University of South Alabama
- University of New Mexico
- UCLA