Human Subject Protection Program
Investigator Guidance
February 18, 2020

CONDUCTING RISK ASSESSMENTS

Introduction

Investigators should understand the concept of minimizing risk when designing research and conduct a risk-benefit assessment. In the protocol the Investigator should:

- Describe potential risks and discomforts associated with each intervention or research procedure;
- Estimate the probability that a given harm may occur and its severity;
- Explain measures that will be taken to prevent and minimize potential risks and discomforts;
- Describe the benefits that may accrue directly to subjects; and
- Discuss and the potential societal benefits that may be expected from the research.

Risks to subjects who participate in research should be justified by the anticipated benefits to the subject or society. This requirement is found in all codes of research ethics, and is a central requirement in the Federal regulations (45 CFR 46.111 and 21 CFR 56.111). Two of the required criteria for granting IRB approval of the research are:

- Risks to subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB Committee will consider only those risks and benefits that may result from the research, as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research.

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: A risk is minimal when “the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater in and of themselves than those ordinarily encountered in *daily life of the general population* or during the performance of routine physical or psychological examinations or tests.” Examples of procedures that typically are considered no more than minimal risk include: collection of blood or saliva, moderate exercise, medical record chart reviews, surveys, quality of life questionnaires and focus groups.

Privacy: Privacy is about people and their sense of being in control of others access to them or to information about themselves.

Confidentiality: Confidentiality is about how identifiable, private information that has been disclosed to others is used and stored. People share private information in the context of research with the expectation that it be kept confidential and will not be divulged except in ways that have been agreed upon.

Types of Risks to Research Subjects

Physical Harms: Medical research often involves exposure to pain, discomfort, or injury from invasive medical procedures, or harm from possible side effects of drugs, devices or new procedures. All of these should be considered "risks" for purposes of IRB review.

- Some medical research is designed only to measure the effects of therapeutic or diagnostic procedures applied in the course of caring for an illness. Such research may not entail any significant risks beyond those presented by medically indicated interventions.
- Research designed to evaluate new drugs, devices or procedures typically present more than minimal risk and involve risks that are unforeseeable that could cause serious or disabling injuries.

Psychological Harms: Participation in research may result in undesired changes in thought processes and emotion (e.g., episodes of depression, confusion, feelings of stress, guilt, and loss of self-esteem). Most psychological risks are minimal or transitory, but some research has the potential for causing serious psychological harm.

- Stress and feelings of guilt or embarrassment may arise from thinking or talking about one's own behavior or attitudes on sensitive topics such as drug use, sexual preferences, selfishness, and violence.
- Stress may be induced when the researchers manipulate the subjects' environment to observe their behaviors and reactions. The possibility of psychological harm is heightened when behavioral research involves an element of deception.

Social and Economic Harms: Some losses of privacy and breaches of confidentiality may result in embarrassment within one's business or social group, loss of employment, or criminal prosecution.

- Areas of particular sensitivity involve information regarding alcohol or drug abuse, mental illness, illegal activities, and sexual behavior.
- Some social and behavioral research may yield information about individuals that could be considered stigmatizing to individual subjects or groups of subjects. (e.g., as actual or potential carriers of a gene; individuals prone to alcoholism). Confidentiality safeguards must be strong in these instances.
- Participation in research may result in additional actual costs to individuals. Any anticipated costs to research participants should be described to prospective subjects during the consent process.

Privacy Risks: Loss of privacy in the research context usually involves either covert observation or participant observation of behavior that the subjects consider private. It can also involve access and use of private information about the subjects. The IRB must make two determinations:

- Is the loss of privacy involved acceptable in light of the subjects' reasonable expectations of privacy in the situation under study; and
- Is the research question of sufficient importance to justify the intrusion?

Breach of Confidentiality Risks: Absolutely confidentiality cannot be guaranteed and is always a potential risk of participation in research. A breach of confidentiality is sometimes confused with loss of privacy, but it is a different risk. Loss of privacy concerns access to private information about a person or to a person's body or behavior without consent; confidentiality of data concerns safeguarding information that has been given voluntarily by one person to another. It is important to recognize that a breach of confidentiality may result in psychological harm to individuals (embarrassment, guilt, stress, etc.) or in social harm.

Conducting Risk Assessments

Role of the Investigator: When designing research studies, investigators are responsible for conducting an initial risk-benefit assessment. Well-designed studies minimize risks to the extent possible and maximize benefits to the subjects.

Role of the IRB: The IRB ultimately 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 of improved health for the research subjects, justifies asking any person to undertake the risks. The IRB cannot approve research in which the risks are judged unreasonable in relation to the anticipated benefits. The IRB must be able to:

- Identify the risks associated with the research, as distinguished from the risks of therapies the subjects would receive even if not participating in research;
- Determine that the risks are minimized to the extent possible;
- Identify the probable benefits to be derived from the research;
- Determine that the risks are reasonable in relation to be benefits to subjects, if any, and the importance of the knowledge to be gained; and
- Assure that potential subjects will be provided with an accurate and fair description (during consent) of the risks or discomforts and the anticipated benefits.

How to Perform a Risk Assessment

Step 1 - Identify and distinguish risks associated with:

- Procedures performed solely for research
- Procedures or therapies subjects would receive even if not in research
- Procedures that are experimental or investigational

Step 2 - Identify the context in which research procedures are performed

- Research procedures added to a conventional (standard) care event

  Examples: extra blood draw at routine draw; additional time in CT scanner for research imaging; additional biopsies; longer anesthesia time to measure O2 saturation levels

Step 3 - Consider the subject population

- Age, health status of subjects
- Subjects who are more sensitive or vulnerable to the risks posed by the research
- Identification and recruitment of subjects
- Additional protections that should be in place to minimize risks and maximize benefits

Methods to Minimize Risks

- Provide complete information in the protocol regarding the experimental design and the scientific rationale underlying the proposed research, including the results of previous animal and human studies.
- 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.
- Collect data from conventional (standard) procedures to avoid unnecessary risk, particularly for invasive or risky procedures (e.g., spinal taps, cardiac catheterization).
- Incorporate adequate safeguards into the research design such as an appropriate data 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.
- Incorporate procedures to protect the confidentiality of the data (e.g., encryption, codes, and passwords) and follow CHLA Information Security requirements.