IRB SOP 507
Risks to Research Subjects

Purpose

The purpose of this Standard Operating Procedures (SOP) is to identify and analyze risks and identifying measures to minimize such risks. This SOP also serves as guidance on how to assess the risk of harm to participants in human research and what procedures should be implemented in order to minimize risk.

Scope

This Standard Operating Procedure applies to all Investigators and IRB members.

Definitions

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

Minimal Risk: A risk is considered to be minimal where 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 or during the performance of routine physical or psychological examination or tests.

Benefit: A valued or desired outcome; although these terms may appear straightforward, evaluations of risk and benefit are made more complex both by the subtle distinctions between therapeutic and research activities, and by evaluations of actual risks in the lives of normal and vulnerable classes of subjects (i.e., prisoners, children, cognitively impaired individuals, etc.)

Policy

1.0 Risk in Human Subjects Research

Risk is the probability of harm or injury (physical, psychological, social, legal or economic) occurring as a result 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). Federal regulations define only "minimal risk".

The IRB will consider a wide range of categories or types of risks including physical, psychological, social, economic, legal or unknown risks. In most cases these risks apply to individuals, however, risks can also apply to groups of individuals (e.g. research on alcoholism among Native Americans may be perceived as reinforcing a negative stereotype). A research procedure or intervention may be minimal risk to certain individuals or groups, but greater than minimal risk to others. For example, the effect on "vulnerable" populations and the specific circumstances of a protocol may change the risk/benefit ratio making the study greater than minimal risk. Many risks in social, behavioral, and educational research are often subjective from the perspective of the participant and the researcher should consider this when evaluating risks. The overall study risk is determined by the risk to the most vulnerable known members of the group

2.0 Types of Risk to Research Subjects

Physical Harms. This would consist of minor pain, discomfort or injury from a procedure during research or device research. The physical harm could be permanent but most are transient in

psychological harm investigators are encouraged to think through all risk possibilities, however rare, so that a course of action can be planned to quickly and effectively minimize the distress

Legal Harms: Many researchers find themselves in ethical and legal quandaries when presented with a subpoena, which is a legal document requesting an appearance in court. While a subpoena is not likely for most research studies, if a study is examining things like sexual abuse, drug use or criminal activity, then it may cause the participants legal harm (consequences). Legal harm can be defined as causing an interaction between the participant and the court system.

3.0

- Provide complete information in the protocol regarding the experimental design and the scientific rationale underlying the proposed research, including the results of previous studies.
- Use procedures which are consistent with sound research design and which do not unnecessarily expose participants to risk.
- 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 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 confidentiality of data (e.g. encryption, codes, passwords) and follow the USA IRB Human Research Data Security Standards.
- Obtain a Certificate of Confidentiality (CoC). This legal document provides protection against compelled (legal demand) disclosure of identifying information about individuals enrolled in sensitive biomedical, behavioral, clinical or other research. CoCs are issued by the National Institutes of Health (NIH) (https://humansubjects.nih.gov/coc/index)
- Obtain HIPPA Authorization or a waiver: Depending on the construct of your research you may request access to one's personal medical records through a HIPPA Authorization form or you may request a waiver of HIPPA under very specific circumstances (see SOP HIPAA in Research).
- Obtain FERPA Consent or waiver: Depending on the construct of your research you may request access to one's education records through a FERPA consent form or you may request a waiver of FERPA under very specific circumstances.
- Obtain signature from the Legally Authorized Representative (LAR) for potential adult participants with diminished decision-making capacity (e.g. result of trauma, mental retardation, forms of mental illness, or dementia). The LAR is an individual, judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research (45 CFR 46.102(c)).

Procedures

These policies and procedures are based on: Common Rule 45 CFR 46.111(a)(1),(2); FDA 21 CFR 56.111(a)(1),(2) When reviewing the application submitted by the Principal Investigator (PI), the IRB analyzes levels of risk, ensures risks are minimized, and ensures risks are reasonable relative to anticipated benefits, before approving the proposed research.

Investigators submitting research proposals for IRB review should understand that the IRB is responsible for assessing the possible risks vs. anticipated benefits, if any, of research as one of its primary functions. In addition, once risks and benefits have been assessed, the IRB is responsible for ensuring that the risks of study participation are minimized to the greatest extent possible, while the benefits of study participation are maximized.

1.0 Identifying Potential Risks (PI Input)

When considering risks, the IRB considers only those risks associated with the research, i.e., physical, psychological, social, legal, emotional. Investigators should be aware that risks would include immediate risks of study participation, risks of randomization (especially to placebo groups in medical and pharmaceutical research), risks of breach of confidentiality, and risks of long-term effects.

For biomedical research (primarily medical and pharmaceutical research) the IRB is required to determine and differentiate between the risks associated with the research and the risks associated with standard diagnostic or therapeutic interventions or therapies subjects would undergo regardless of participation in research. The IRB does not establish or determine what constitutes “standard of care.” It is important for investigators to clearly distinguish procedures which they consider are “standard of care” from those which are conducted solely for research purposes in the protocol and the informed consent form.

Minimal Risk Much of the IRB review process is governed by the concept of “minimal risk.” Assignment of research for expedited review, approval of waiver of consent, and the conduct of research involving vulnerable research populations may be dependent upon whether the research places subjects at minimal risk or greater than minimal risk (significant risk).

2.0 Ensuring Risks Are Minimized (IRB Determination)

The IRB considers the overall level of risk to participants in evaluating the proposed research in accordance with the conditions outlined in 45 CFR 46.111(a)(2), 21 CFR 56.111(a)(1), and the ethical principles outlined in the Belmont Report. Furthermore, the IRB may consult with additional experts as needed. [45 CFR 46.111(a)(1)(i), 21 CFR 56.111 (a)(1)(i)]

When assessing risks and benefits, the IRB is required to:

1. identify the risks associated with the research, as distinguished from the risks of therapies the subjects would receive even if not participating in the research;
2. determine that the risks will be minimized to the fullest extent possible;
3. identify the probable benefits to be derived from the research;
4. determine that the risks are reasonable in relation to the benefits to subjects, if any, and the importance of the knowledge to be gained;
5. assure that potential subjects will be provided with an accurate and fair description of the risks or discomforts and the anticipated benefits;
6. determine intervals for periodic review (no greater than annually), and, where appropriate, determine that adequate provisions are in place for monitoring the data collected and, if the subjects are likely to be members of vulnerable populations, determine that appropriate additional safeguards are in place to protect the rights and welfare of these subjects.

The IRB examines the research plan, including research design and methodology, to determine that there are no inherent flaws that would place research participants at unnecessary risk. This includes the risk that research lacking in statistical power may not lead to meaningful results. Appropriate safeguards can also minimize risk to participants, for example: having an adequate data monitoring plan, or protecting confidentiality by using coded data. If risks are not adequately minimized, the protocol will not be approved as written.

The IRB also considers the professional qualifications and resources (including time, equipment, support services) of the research team to protect participants and minimize potential harm. Research personnel must have received appropriate training, and clinicians involved in the research must maintain appropriate professional credentials and licensing privileges.

3.0 Data Monitoring Plan (Required for Greater Than Minimal Risk Studies)

To approve research, the IRB must determine that, where appropriate, the research plan makes adequate provisions for monitoring the data to ensure the safety of research participants. (45 CFR 46.111(a)(6), 21 CFR 56.111(a)(6), 38 CFR 16.111(a)(6))

Many studies (e.g., if more than minimal risk) need a Data and Safety Monitoring Plan (DSMP):

Data Monitoring Plans and Data Monitoring Committees – NIH and NCI policies:
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IRB Review of the Data Monitoring Plan (See SOP: Data Safety Monitoring Plan)

In addition, periodic (usually annual) reports from the monitoring entity are submitted by the PI to the IRB at continuing review. (When a monitoring entity is used, the IRB conducting continuing review of the research may choose to rely on a current statement from the monitoring entity indicating that it has and will continue to review study wide adverse events, interim findings, and any recent literature that may be relevant to the research.)

Whether the method of monitoring is by PI oversight or the establishment of a DSMB, the IRB can tailor a specific timeframe for future reporting of data monitoring findings to the IRB. The IRB can set the date of continuing review for the protocol as being less than the maximum of a year, if they determine that interim reporting of data monitoring information will serve to better protect participants. Alternatively, the IRB can request a report after a specific number of participants are enrolled or after a serious adverse event has been reported.

4.0 Risks to Vulnerable Populations

The IRB is cognizant of the vulnerable nature of many participants. Food and Drug Administration (FDA) regulations and the Common Rule require IRBs to give special consideration to protecting the welfare of vulnerable participants. In order to approve research involving vulnerable populations, the IRB must determine, where appropriate, that additional safeguards have been included to protect the rights and welfare of participants who are likely to be vulnerable to coercion or undue influence, such as:

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