

5 Risk Benefit Assessment

Investigators submitting research proposals for IRB review should understand that the Committee is responsible for assessing the risks vs. anticipated benefits 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 the study participation are minimized to the greatest extent possible while the benefits of the study participation are maximized. This is clearly stated in all codes of research ethics and is incorporated throughout the federal regulations that govern the IRB.

The following definitions of risk, minimal risk and benefit, which are used to assess risks and benefits as they pertain to research conducted at Sunrise Health, are defined by the Department of Health and Human Services (DHHS) as follows:

Risk: The probability of harm (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. The federal regulations define only “minimal risk” (see below).

Minimal Risk: A risk is 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 examinations or tests [45 CFR 46.102(i)].

Benefit: A valued or desired outcome; and advantage.

Although these terms may appear straightforward, evaluations of risk and benefit are made more complex both by 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.).

It is important for investigators to understand that the comparison between risks and benefits is not a comparison between identical concepts. Because the term “Risks” is normally expressed as probabilities while the term “Benefits” is normally expressed as fact or a current state of affairs, investigators may find it difficult to compare these concepts in a meaningful fashion. Therefore, it is more convenient for researchers to think of these terms as evolving probabilities. For example, the risks of participation in research can be expressed as a probability that subjects may be harmed by research procedures while anticipated benefits may express the probability that subjects and society may benefit from research procedures. By considering risks and benefits as probabilities, the IRB evaluation process is also simplified.

IRB CONSIDERATIONS

There are a number of steps discussed by the DHHS that the IRB must follow when assessing risks and anticipated 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 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 of periodic review, and, where appropriate, determine that adequate provisions are in place for monitoring the data collected, and where the subjects are likely to be members of a vulnerable population, determine appropriate additional safeguards are in place to protect the rights and welfare of these subjects.

Because the IRB is required to follow the above listed procedures, investigators should address these considerations in their consent.

IDENTIFICATION AND ASSESSMENT OF RISKS

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), risks of breach of confidentiality, and risks of long term effects.

For biomedical 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. Since the IRB does not establish or determine what constitutes standard of care, it is important for investigators to clearly distinguish procedures which are standard of care from those which are conducted solely for research purposes in the protocol and the informed consent form.

Physical Risks

Some biomedical research presents risk of physical injury to subjects. Although most of these risks are transient, some adverse effects of study participation (especially those which result from medical procedures, drug research or device research) may result in permanent injury to subjects. For all research with the potential to cause physical harm investigators are encouraged to think through all risk possibilities, however rare, so that they can be resolved quickly and effectively minimize the harm to subjects. By clearly detailing procedures to address situations of physical harm, the IRB can be assured that the investigator has made efforts to minimize physical risks to the greatest extent possible.

Psychological Risks

Some research has the potential to cause undesired changes in thought processes and emotion including episodes of depression, confusion, and hallucination resulting from drugs, feelings of stress, guilt and loss of self esteem. As is the case with physical risks, these effects are usually transient. For all research with the potential to cause 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 to subjects. By clearly detailing procedures to address situations of psychological harm, the IRB can be assured that the investigator has made efforts to minimize psychological risks to the greatest extent possible.

Social and Economic Risks

Some research proposals involve the handling of sensitive information which may result in injury to subjects through a breach in confidentiality. These breaches may result in embarrassment within a subject's business or social group, loss of employment, or criminal prosecution. The IRB is especially concerned about information regarding drug and alcohol use, mental illness, sexual behavior and illegal activities. For these situations, investigators should clearly detail strong safety precautions to ensure that the research does not cause social or economic risks to the subjects.

Research may also pose direct economic risk to study subjects. Procedures billed to insurance companies may require a significant co-payment on behalf of the subjects, insurance companies may refuse to pay for "investigational" therapies, subjects may be responsible for transportation costs, and subjects may lose wages during research participation. Investigators should attempt to minimize economic costs to the individuals; the anticipated costs should be described to subjects during the consent process.

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). Investigators should note that studies proposing procedures which pose less risk than standard procedures may not necessarily be determined to be of minimal risk to subjects. Investigators should pay particular attention to the term minimal risk as it is applied throughout this manual. **NOTE: When the risks are unknown, they are considered greater than minimal.**

BENEFITS

The benefits of research fall into two categories: benefits to individuals and benefits to society.

Research frequently provides subjects with treatment, diagnosis or examination for an illness or abnormal condition. In these cases the research involves evaluations that may benefit the subjects by ameliorating their condition or provide a better understanding of their disorder. Investigators should clearly detail these potential benefits for the IRB, in the application, and subjects, in the consent form, while not overstating these benefits. The investigator should also attempt to maximize benefits to the greatest extent possible for potential subjects.

Although research may not always provide a benefit to society, researchers are encouraged to design research projects so that information, in the form of generalizable knowledge, can contribute to societal benefit whenever possible. Investigators should clearly detail these potential benefits for the IRB, in the application, and for subjects, in the consent form, while not overstating these benefits. Research which does not provide benefit to individuals is required to provide a reasonable likelihood of resulting in benefits for society.