

Guidance University of Kentucky Assessing the Research Risk

Determining the proper risk classification of a research protocol is an important aspect of the review by an Institutional Review Board (IRB). The risk classification may influence the mode of review (expedited vs. convened board), whether or not a protocol can be approved by the IRB (if children or prisoners are involved, whether or not it must be sent to the DHHS Secretary), the frequency of review, consent requirements (e.g., waiver of informed consent or documentation of informed consent), and several other factors.

1. Definitions

Minimal Risk:

- a) *Minimal Risk* means that 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. [\[45 CFR 46.102\]](#)
- b) *Minimal risk* is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons. [\[45 CFR 46.303\]](#) (This definition only applies to research involving prisoners.)

The definition of minimal risk provided by the federal regulations invites interpretation which may lead to inconsistencies among IRB and reviewers. This document provides guidance for IRB reviewers.

2. Identifying and Evaluating the Research-Related Risks

- a) IRB reviewers should be diligent to focus only on the risks associated with the protocol that are **directly related to the research**. Risks associated with the standard of care procedures that may provide the framework for the research should not factor into the risk classification. *In evaluating risks and benefits, the IRB should 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) [\[45 CFR 46.111 \(a\)\(2\)\]](#)*
- b) The IRB should concentrate on the **immediate or reasonably foreseeable risks of the research** rather than the risks associated with the long-term outcome or consequences of applying the knowledge gained from the research. *The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility. [\[45 CFR 46.111\(a\)\(2\)\]](#)*
- c) In identifying risks, the IRB should consider a wide range of categories regarding types of risks. For example, risks can be physical, psychological, social, economic, legal or unknown.
- d) In identifying risks, the IRB should consider that risks can apply to individuals. When applicable, the IRB should also consider risks that apply to classes of participants (e.g., research on alcoholism in Native Americans).

3. Interpretation of Minimal Risk as Defined in 45 CFR 46

Classifying the risk category is not an easy task. In 2001, the National Bioethics Advisory Commission (NBAC) recommended using a minimal risk standard related to the **risks of daily life that are familiar to the general population**. Studies involving a level of risk no greater than that encountered in the daily lives of those in the general population may be considered minimal risk. The Department of Health and Human Services (DHHS) Secretary's Advisory Committee on Human Research Protection (SACHRP) recommended in 2005 that DHHS use a "healthy" person standard when applying [45 CFR 46 Subpart D](#) (i.e. research involving children). University of Kentucky IRB policy also recommends that the IRB use a healthy person standard when applying the federal definition of "minimal risk" in research in children unless investigators can justify the use of a relative standard.

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4. Minimal vs. Greater Than Minimal

Once the risks associated with the research have been identified, the process of categorizing the risks as *minimal* or *greater than minimal* may begin. Two characteristics influence the nature of the risk: 1) the **probability** of harm; 2) the **magnitude** of harm. The magnitude of harm can be related to the severity, duration and reversibility of a potential harm. The IRB reviewer should consider both the likelihood and magnitude of harm and whether they are greater than those encountered in daily life or during routine physical or psychological examinations.

5. Minimizing the Risks : Impact on Minimal Risk Assessment

An aspect of risk assessment that is often overlooked is what protections are in place to minimize the harm. An IRB may diminish the risks to subjects by minimizing the probability and/or magnitude of harm to subjects. A greater than minimal risk may be reduced to minimal risk if protections are adequate to protect participants. For example, a breach of confidentiality is a serious risk, but protections such as restricted access, encryption, and/or Certificates of Confidentiality reduce the absolute risk significantly and may thereby make the overall risk to the participant minimal.

6. Minor Increment Over Minimal Risk (for research involving children):

The IRB's determination to approve a study as "minor increment over minimal risk" is a subjective decision and the IRB should review each study on a case by case basis. The IRB may use the following criteria to help determine whether a risk is slightly more than minimal:

1. The procedure does not meet the "minimal risk" criteria;
2. The increase of the probability and magnitude of harm is only slightly more than "minimal risk";
3. Any harms associated with the procedures would be transient (restricted to time of procedure or short post-experimental period) and reversible (requiring no more than a short post-experimental clinical intervention);
4. There is no or an extremely small probability that the potential pain, discomfort, stress or harm associated with the procedure(s) which the subject might experience would be severe.

[These criteria were adapted from DHHS SACHRP 2005 recommendations on Subpart D.]

7. Risk/Benefit Ratio Assessment

An IRB reviewer identifies any risks involved with the study and classifies those risks as minimal or as greater than minimal risk, weighing the benefits of the study against those risks. The IRB reviewer then assesses whether the risk to participants are **reasonable** in relation to the anticipated benefits to participants, if any, and the importance of the knowledge that may reasonably be expected to result. The use of "vulnerable" populations and the specific circumstances of a protocol may change the risk/benefit ratio making the study greater than minimal risk.

The benefits of a study do not alter the risk classification. The risk/benefit assessment only refers to the acceptability of the risk, not the level of the risk. A study deemed greater than minimal risk cannot be classified as minimal risk because the potential benefits are great, but it could be approved for this reason. Whereas, the same greater than minimal risk study may not be approvable if the benefits are lacking. An IRB reviewer should disapprove research in which the risks are judged to be unreasonable in relation to the anticipated benefits (OPRR IRB Guidebook, '93).

In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied: (2) 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. [\[45 CFR 46.111: \(a\)\]](#)

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