To What Extent Do Risks Need to Be Minimized?

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Dear Practical Ethicist,

Our Institutional Review Board (IRB) sometimes struggles with the application of the regulatory criterion that for clinical research to be approvable, risks should be minimized. Some members believe that this means that risks should be absolutely as low as possible, to the point of recommending that procedures be removed from the protocol unless they are necessary for monitoring participant safety. Other members are much more comfortable with risk and focus more on the criterion of whether the risks are reasonable in relation to the anticipated research benefits. How do we reconcile these positions? To what extent do risks need to be minimized to make research ethical?

Sincerely,
Research Is So Critical

Dear RISC,

To approve research, IRB/Research Ethics Boards (REBs) have to determine that risks to subjects are minimized (a) using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk, and (b) whenever appropriate, using procedures already being performed on the subjects for diagnostic or treatment purposes (Institutional Review Boards, 2009; Protection of Human Subjects, 2009).

When the research involves no more than minimal risk to subjects, IRB/REBs can consider the criterion on minimization of risk to be met. There is no ethical mandate to reduce research risk to less than the level of risk that is encountered in daily life.

Although the criterion described above is often abbreviated to "risks must be minimized," this criterion is not a mandate for IRBs to determine that risks to subjects are minimized to the absolute greatest extent possible. The risks of research can always be completely minimized by not allowing the research to proceed. Instead, this criterion describes the minimization of risk by considering two strategies: (a) using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (b) using procedures already being performed on the subjects for diagnostic or treatment purposes. IRB/REBs dealing with a difficult protocol can find it useful to revisit the language of the entire criterion.

This criterion is also independent of the consideration of benefits. If risks are reasonable in relation to benefits but the criterion on minimizing risks itself is not met, the research cannot be approved. IRB/REBs dealing with a difficult protocol may find it helpful to consider this criterion independent of other criteria related to risk. It is best to consider this criterion in advance of other criteria related to risk, because if the IRB/REB decides that changes to the research are necessary to reduce risk, these changes have a downstream effect on the other criteria related to risk.

The concept of minimizing risk using procedures already being performed on the subjects for diagnostic or treatment purposes is straightforward. IRB/REBs can assess whether there are any research procedures that can be combined with procedures that are being performed for non-research reasons in a way that the added risk of the research is reduced. If it is reasonable to reduce risks in this manner, then the protocol needs to be modified accordingly as a condition of approval.

The concept of minimizing risk using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk is more difficult. IRB/REBs can consider whether there is another way to conduct the research that reduces risk (without increasing other risks), where those procedures are scientifically valid. That is, using those alternate procedures still allows the research study to answer the scientific question being posed. If it is possible to use different and less risky procedures and to obtain equally-valid scientific results, then the risk has not yet been minimized using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk. The IRB/REB needs to require the alternate procedures as a condition of approving the research.

With greater than minimal risk—and particularly with potentially high risk—studies, IRB/REBs understandably want to find ways to reduce risk. When every potential strategy the IRB considers to reduce risk adversely affects the scientific design of the study, IRB/REBs need to accept that this criterion is met and evaluate risks using the other criteria for approval that assess risk. This concern often arises with placebos, washout periods, sham procedures, and sham devices. IRBs cannot use this criterion to change protocols to have unsound design simply to reduce research risks. Again, IRB/REBs reviewing protocols with these issues can benefit with a focused discussion of this criterion independent of all others.

There are a few other considerations that affect how IRBs assess and discuss the concept of "risk." Risk is the

probability of harm. Harm is actual damage or injury. Individuals can be put at risk and never experience harm. Risk can be characterized by both the probability that the harm will occur and the magnitude (intensity, extent, or severity) of the harm. Risks can be reduced either by reducing the probability of harm, by reducing the magnitude of harm, or both. In considering the study procedures, either of these may be a way to reduce risk. Psychology experiments have shown that humans are poor at estimating the true probability of harm (Sutherland, 2007). People tend to overestimate the risks of things that are unfamiliar to them and to underestimate the risks of things that are familiar. They assign lower probabilities of harm to their own actions and higher probabilities of harm to the actions of others. For this reason, whenever possible, IRB/REBs should use real data to assess probability of harm. Literature searches can often elucidate the probabilities of, for example, the risk of bone fracture in childhood (about 2%/person/year; Erik & Waernbaum, 2014) or the risk of a breach of confidentiality of financial records (about 7%/person/year; Bureau of Justice, 2015).

Minimizing risk is always a judgment call. IRB/REBs can always reduce risk by requiring 23 gauge instead of 21 gauge needles for venipuncture, requiring the surgeon to have six years of experience instead of five, having two nurses monitor each subject instead of one nurse. Even if the change is consistent with sound research design, the true reduction in risk may be trivial. IRB/REBs must be realistic in determining whether a reduction in risk is actually a meaningful reduction in risk.

In summary, the criterion the IRB/REB should follow is to minimize risk by (a) using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk, and (b) using procedures already being performed on the subjects for diagnostic or treatment purposes. Risks must be assessed in terms of probability and magnitude. Find and use empirical data wherever possible to determine probability. For greater than minimal risk research, determine whether there is a different way to do the research that involves less risk but does not adversely affect scientific design, or whether risks can be reduced to a material extent by combining clinical and research procedures. If not, this criterion is met. With difficult protocols, deliberate separately on the full wording of this criterion.

P. Ethicist

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Author Biographies

Practical Ethicist, in real life, is a collaboration of two experts: Jeffrey A. Cooper and Lindsay McNair. They can be reached at JCooper@wcgclinical.com and LMcNair@wcgclinical.com.

Jeffrey A. Cooper, MD, MMM, is a physician, basic science investigator, clinical investigator, and manager with many years of ethical review experience as a member and chair of an IRB. He left medical practice in 2002 to help the Association for Accreditation of Human Research Protection Programs, Inc. (AAHRPP), where he was responsible for the development and operation of the accreditation process. He is currently the vice president for process and strategic improvement for the WIRB-Copernicus Group.

Lindsay McNair, MD, MPH, MSBioethics, is a physician, clinical investigator, and former academic IRB member who has spent most of her career working in clinical research for the pharmaceutical and biotechnology industry, with a specific interest in ethical drug development research. She is an adjunct faculty member at Boston University and is currently the chief medical officer for the WIRB-Copernicus Group.