IRB *EasyEd™* - For IRB Members Volume 1 Number 6

Topic: Assessing Scientific Validity

Overview of the Topic

Much to the chagrin of many investigators, and probably some IRB members, the IRB has the responsibility to assess the scientific validity of proposed research. This charge is related to the regulatory determinations required for approval of research and to the IRB's ethical responsibilities to protect subjects. Of course, for as many people as will criticize the IRB for performing scientific review, there are many others who will find fault with IRBs for not providing enough scientific scrutiny and approving poorly designed research, pointing out that it is the IRB's obligation to conduct such review.

The Nuremburg Code (1949) stated that "*The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature*." The first basic principle of the Declaration of Helsinki (1964) is that "*Research involving human subjects must conform to generally accepted scientific principles*." These principles obviously apply to human research in general, and not specifically to IRB responsibilities, although one could argue that the IRB should not approve research that does not meet these principles.

The first criteria for IRB approval of research according to the US regulations is that "Risks to subjects are minimized by using procedures which are consistent with sound research design and whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes." (45CFR46.111(a)1). To fulfill this purpose the IRB must look at the "procedures" involved in the research and the soundness of the research design. Now, the IRB can perform the assessment of scientific validity itself, or it can be provided the information from another source, such as a scientific review committee or departmental review. If the latter occurs, the IRB must be provided with the results of the scientific review in sufficient detail for the IRB to make its required regulatory determinations. The scientific review external to the IRB should be thorough, not merely the signature of an administrator such as a department chair. Many organizations do not have these other scientific review mechanisms, some for practical or resource reasons and some because they do not want to question the science of their "experts." The latter is an erroneous position because all research proposals benefit from critical review and improvement. Nevertheless, in these situations the task of scientific review falls to the IRB to perform.

The philosophy is that if research is poorly designed, poorly carried out, or not likely to produce valid results, no risk to human subjects is acceptable. Of course the application of this principle is related to the degree of risk. A poorly designed record review project by a medical resident, or a low risk survey by a graduate student that most likely would not yield any meaningful results may require less attention than higher risk research (although ideally someone in the organization should have the responsibility to educate neophyte researchers to design more meaningful research as well as appreciate the protection of human subjects). In addition to the risks to subjects, poor research may produce misleading results and may become directly or indirectly harmful to science or and may lead to ineffective services, interventions or treatment. One can relate this to the adage, "Garbage in, garbage out!" both in terms of individual projects and the impact on science in general.

Here are some points to consider when the IRB (or another entity) conducts an assessment of scientific validity. Of course this list is not exhaustive and does not account for the many different types of research that IRB review (for example ethnography or historical research). However these issues will generally apply to much research (but be flexible when it does not).

1. **Knowledge of the field, background information, and preliminary results** – Has the researcher displayed knowledge of the field, provided adequate background with an appropriate number of references, and has developed this protocol in regard to the state of knowledge? Is there preliminary data to support the research question?
2. **Hypotheses or Research Questions** – Are the hypotheses or research questions clearly stated and appear sound and reasonable?

3. **Methodology** – Is the methodology well thought out and sound and consistent with methods used in the field? Is the proposed subject population appropriate?
4. **Sample size and Statistical Analysis** – Are statistical considerations, including sample size and justification, estimated accrual and duration, and statistical analysis clearly described and adequate to meet the study objectives?
5. **Significance**, B**enefit and Risk** – Has the investigator adequately articulated the significance of the research, and whether the benefits (either to the participants or science/society) clearly outweigh the risks to human subjects?
6. **Qualifications of the investigator and Research Team** – Does the investigator and research team have the skills, capacity, and experience to carry out this project? A procedure may be great and appropriate, but if the investigator is not qualified to perform the procedure, the results may be dubious.
7. **Resources** – Will the investigator be provided with, or obtain (e.g. grant), adequate resources to conduct the project and protect human subjects before the project commences?

Many IRBs would add the question "What is the importance of the knowledge expected to result from the research?" and "Will the research provide important knowledge to the field?" These are much more difficult questions for the IRB to answer for several reasons. One, you do not know what the results may be. The most promising study may yield negative results and a simple study may produce surprising and important results. As Einstein said, "If we knew what we were doing, it wouldn't be called research." Secondly, while the IRB may have one or more experts in the particular "field," they do not speak for the "field." The science in the "field" moves forward only after many research publications, usually with differing results, are analyzed and culled, more weight is given to one theory than another, and the "field" moves forward in the most widely accepted direction. You can see why the IRB cannot make this type of decision. But as described above, the IRB can make determinations about the procedures being appropriate and the research being well designed and minimizing risks to research participants.

Questions for the IRB to Consider

IRB Decision: When reviewing a research protocol, the IRB must conduct or receive a scientific review which, at the minimum, allows the IRB to answer the following questions related to the regulatory criteria for approval on risk:

1. Is the investigator using procedures that are consistent with sound research design?
2. Will the research design permit the investigator to answer the research question?
3. Is the investigator using procedures that do not unnecessarily expose subjects to risk?
4. Are risks to participants are reasonable in relation to anticipated benefits, if any, to participants and the importance of the knowledge that may reasonably be expected to result.

Case Studies

1. An investigator proposes what you believe is an unreasonably high sample size. **What questions might you ask her?**
2. A PhD kinesiologist proposes to do a study involving treadmill exercise in elderly subjects. **What questions might you ask him?**
3. A researcher proposes research that is greater than minimal risk but has only a cursory plan to protect human subjects. **What would be your approach?**
4. A researcher proposes an interview survey with sensitive questions but plans to conduct it in a patient waiting room because he has no other space in his office. **What are your concerns and what would you require?**
5. An investigator proposes a novel intervention for domestic violence, and while it seems like a good idea, it has never been tried and there is no preliminary data. **Would you approve the study? If not, what tack might you take?**

Prospective Thinking: Have a discussion with your IRB about whether or not you believe you conduct adequate review of scientific validity of research projects. Discuss what improvements you can make in scientific review.