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Scientific Review of Human Subjects Research

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One of the key principles of ethical research involving human subjects is that it should be scientifically rigorous (Levine 1988, Emanuel et al 2000). Scientific validity is important so that research studies will not unnecessarily expose human subjects to risks (Emanuel et al 2000). Research should address important scientific questions.

Regulations and guidelines require that the research risks be reasonable in relation to the benefits to the subjects or to society by means of the knowledge that is expected to be gained (Emanuel et al 2000). If a study is unlikely to produce useful scientific results, there is no acceptable level of risk to the subjects (Council for the International Organisations of Medical Sciences 2002).

A poorly designed study might fail to yield useful knowledge, which undermines the ethical justification for exposing human subjects to risks. For example, in 2001, Ellen Roche, a healthy volunteer, died from inhaling hexamethonium as part of an asthma study conducted at Johns Hopkins University. An investigation of this tragedy by the Office of Human Research Protections found that the researchers had not adequately reviewed previous research on the dangers of inhaling this drug, published in the 1950s and 1960s (Savulescu and Spriggs 2002). In other words, the study was not ethically justifiable because the scientific literature indicated that the research design did not include adequate safeguards to protect subjects from the risks associated with inhaling hexamethonium.

Because committees overseeing the ethical aspects of human research, such as institutional review boards (IRBs) (or research ethics committees (RECs)), might lack the expertise, resources or time to conduct a competent review of the scientific aspects of a proposed study, some institutions have established separate scientific review committees (SRCs). For example, the National Institutes of Health (2013) requires that intramural research involving human subjects undergo scientific review prior to IRB review, although clinical directors may decide that natural history or training studies do not require pre-IRB scientific review. The ethics committee should use the SRC's report to evaluate the scientific and ethical aspects of the proposed study.

To be useful to an IRB, the SRC's report must contain the information the committee needs to review ethical aspects of the study, such as a scientific evaluation of the study's design, risks, benefits and measures used to minimize risks. An SRC may also comment on non-scientific issues, with the understanding that the IRB has final jurisdiction over ethical and regulatory aspects of the research.

Although the investigator provides scientific information and analysis concerning the study to the IRB, a scientific perspective independent of the investigator can be worthwhile, since the investigator's knowledge might be insufficient or judgment might be flawed, perhaps because of bias. For example, an investigator might underestimate the risks associated with a study or overestimate the benefits to secure IRB approval. Additionally, the investigator might be more likely to respect the scientific judgment of an SRC than that of an IRB without significant and relevant scientific expertise. Figure 1 presents questions that the investigator and the SRC should both answer for the IRB.

Just as the SRC should respect the IRB's jurisdiction, the IRB should respect that of the SRC. While IRBs have the authority and responsibility to review any aspect of research that pertains to the rights, safety or well-being of human subjects (Emanuel et al 2000),

performing duplicative scientific reviews or second guessing the SRC's findings might make SRC members wonder if they are wasting their time. Investigators might also question the IRB's opinions on scientific issues. However, the IRB might have expertise not available to the SRC, notice something the SRC missed, or just have a different perspective. When the IRB disagrees with the SRC's report, it should explain its reasoning to the SRC so the committees can learn from each other, work together more effectively in the future, and not attract attention from institutional officials who might view the IRB's forays into scientific review as a form of "mission creep" or an opportunity to streamline the organization (Gunsalus et al 2006).

Figure 1. Scientific Review Form

The purpose of this form is to provide the IRB with information and analysis concerning the scientific aspects of the proposed study, which it can use to evaluate the ethical and regulatory aspects of the research. Answer each question from a scientific perspective and, where appropriate, provide commentary to explain your answer.

1. Does the proposed study address an important scientific, medical, public health, or social question or issue?
2. Does the study address questions not already addressed adequately by previous studies?
3. Is the study likely to make a significant contribution to the literature?
4. Are the aims, objectives and hypotheses clearly stated?
5. Is the study well-designed?
6. Are the methods and procedures appropriate?
7. Are the inclusion/exclusion criteria appropriate?
8. Are the statistical methods appropriate?
9. Is the study adequately powered?
10. Are study personnel qualified to perform the research?
11. Will any collaborating investigators or institutions provide scientific expertise, data, samples, or other help in conducting the research?
12. Are the personnel, facilities, funding and other resources adequate to conduct the research?
13. Does the proposal include an adequate review of prior research pertaining to the study?
14. Does the proposal include adequate plans to publish the research and share data, samples or results?
15. Is the proposal clearly written?
16. Have the investigators submitted all required documentation, such as radiation safety review and biohazard safety review?
17. Does the proposal clearly identify and describe risks to subjects or others?
18. Does the study use appropriate methods or procedures to minimize risks?
19. Does the study use any investigational drugs or devices? If so, has the investigator submitted adequate documentation from the FDA or other regulatory authority?
20. Does the study involve drug dosing? If so, are the dosing amounts, schedules, sites and routes appropriate to minimize risks?
21. Does the study need a data and safety monitoring board?
22. Does the proposal clearly identify and describe potential benefits to the subjects or others?
23. Are there any other issues that might affect the scientific validity of the study?
24. Should the study be approved as is, approved with modifications, disapproved or tabled due to lack of sufficient information?

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