



## RESEARCH DESIGN

Adapted from Amdur, Robert J., M.D. & Bankert, Elizabeth A. *Institutional Review Board: Management and Function (2005)*. Jones & Bartlett Pub; 2 edition.

### Introduction

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“It is not unusual for institutional review board (IRB) members, institutional officials, and researchers to debate the role of the IRB in evaluating study design or other aspects that affect the fundamental quality of the science of research... Some members of the research community are under the impression that it is not the role of the IRB to evaluate the quality of the science of a protocol... There is no question that the IRB not only has the authority to evaluate scientific quality, but also has the obligation to do so if it is to function in compliance with accepted ethical codes and federal research regulations” (Amdur 2005).

### Ethical Codes

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**Nuremberg Code (1949):** “The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.”

**Declaration of Helsinki (2000):** “(11) Medical research involving human subjects must conform to generally accepted scientific principles and be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, where appropriate, animal experimentation... (18) Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers... (29) The benefits, risks, burdens, and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic, or therapeutic method exists.”

### Federal Research Regulations

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**45 CFR 46.111, Criteria for Approval of Research:** “(a)(1) Risks to subjects are minimized by using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk. (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. 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 research).”

### Scientific Quality and the IRB’s Responsibility

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It is the obligation of the IRB to consider the study design and overall quality of a study in order to effectively evaluate the risk-benefit ratio. If the IRB cannot determine that the risk-benefit ratio of a study is acceptable, it cannot approve the protocol under applicable ethical codes and regulations.

Much of the value of research depends on the integrity of the study results. One of the ethical justifications for research involving human subjects is the social value of advancing scientific understanding and promoting human welfare by improving health care or social understanding. But, if a proposed research study is methodologically flawed to the point that no meaningful or reliable information will result, it is unethical to expose subjects to any level of risk or inconvenience by including them in the research study.

The University of Utah IRB uses the individual and collective judgment of its members when considering whether or not to approve a study based on scientific design. Although IRB members do not need to be experts in scientific methodology or statistics, members understand

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the fundamentals of experimental design, and do not hesitate to consult experts when aspects of research design seem to pose a significant problem. Researchers can assist in this process by carefully considering whether or not the design of their study will adequately answer the research question. Researchers may want to consider having their research proposal design evaluated by a representative of their own department before they submit their protocol to the IRB.

The IRB recognizes that certain circumstances may warrant approval of research where the study design is not preeminent, but where the risks to participants are virtually non-existent (e.g. social science research submitted by students). In these situations, it is reasonable for IRB members with knowledge about these types of research to make suggestions or require revisions to the study plan. Each of these cases is thoughtfully evaluated on a case-by-case basis.

### Additional Considerations

When considering the research design of your proposal, evaluate whether or not each of these questions has been adequately communicated to the IRB in such a way that they will be able to easily recognize them. Clarifications from board members are often the result of inadequate or unclear description in the Application and/or Consent Document(s).

1. Is the scientific design adequate to answer the questions posed?
2. Is the available clinical and non-clinical data on an investigational product adequate to support the proposed clinical trial?
3. Is the sample size (number of participants) adequate?
4. Is the method proposed for selecting and assigning subjects to treatment groups unbiased?
5. Does the investigator serve a dual role that may pose a conflict of interest?
6. Is any of the information to be collected sensitive (e.g., related to sexual practices, substance abuse, or illegal behavior)?
7. Are there adequate plans to protect participants from the risks of breach of confidentiality and invasion of privacy?
8. Are there plans for approaching potential participants in a way that will respect their privacy and their right to decline or refuse to participate? If the protocol involves an epidemiologic study, will participants or their relatives be protected from learning inappropriate information? (*See IRB Investigator Guidance Series: Genetic Research.*)
9. Does the recruitment process protect subjects from being coerced or unduly influenced to participate? Are any payments to participants reasonable in relation to the risks, discomfort, or inconvenience to which participants will be exposed?
10. Are there adequate plans to exclude participants who are vulnerable to injury during the period of withdrawal of active and effective therapy, if that is part of the research design?
11. Have the rights and interests of vulnerable subjects (e.g., desperately ill persons) been adequately considered?
12. Do the consent documents describe the study design (including plans for randomization, use of placebos, and the probability that the subject will receive a given treatment) and conditions for breaking the blinding of the study (if the study is blinded)? Are the descriptions provided at the level the participants can understand?
13. Do the consent documents describe the risks and benefits of each of the proposed interventions and of alternative courses or actions available to the participants?
14. Do the consent documents clearly describe the extent to which participation in the study precludes other therapeutic interventions?
15. Are provisions made for supplying new information to participants during the course of the study and for obtaining continuing consent, where appropriate?
16. Must investigators obtain consent before reviewing records?
17. Will the consent process take place under conditions most likely to provide potential subjects an opportunity to make a decision about participation without undue pressure?

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18. If the study is a clinical trial, how will the trial be monitored? What will be done with preliminary data? Should an independent data and safety monitoring board be established? How will decisions about stopping the trial be made? By whom? On what basis? (See *IRB Investigator Guidance Series: Elements of a Data Monitoring Plan and Elements of a Safety Monitoring Plan*)

#### References & Links

45 CFR 46 <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>

Declaration of Helsinki <http://www.cirp.org/library/ethics/helsinki/>

Nuremberg Code <http://history.nih.gov/research/downloads/nuremberg.pdf>

Investigator Guidance Series:  
*Genetic Research; Elements of a  
Data Monitoring Plan; Elements  
of a Safety Monitoring Plan* <http://irb.utah.edu/guidelines/investigator.php>

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