Announcements

IRB Reviewers - Microsoft Internet Explorer

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Office of the Institutional Review Board

Templates Available:
- IRB Investigators' Template for New Applications
- IRB Investigators' Template for Amendments
- IRB Investigators' Template for Renewals/Continuing Review

Board Education:
- Session #1
Why Today’s Topic

- University of Washington
- Six committees
- 5,000 applications per year.
- OHRP reviewed
  - 38 full board or expedited studies
  - 30 exempt studies

4/20/05
OHRP findings

- IRB at UW "often seem reluctant to defer approval of a study" despite "substantive questions" about the risks and benefits to subjects.
- IRB granted contingent approval for research pending major changes instead of deferring approval until the committees confirmed the changes. As a result, in several instances the committees did not "fully determine" whether the subjects' safety was protected.
Criteria For Approval

45 CFR 46.111
25 CFR 56.111

- Minimized risks
- Reasonable risk/benefit ratio
- Equitable subject selection
- Informed consent process
- Informed consent documentation
- Data monitored for safety
- Confidentiality/privacy maintained
- Vulnerable populations protected
Review Criteria

45 CFR 46.111
21 CFR 56.111

(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 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.
• 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.

• NB: benefits do not have to “**outweigh**” risks.
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).
NB: This means that the risks and benefits of the research have to be clearly differentiated from risks and benefits of clinical care!!
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.
Ethical Basis: Belmont Principle – Beneficence

- The assessment of risks and benefits requires a careful arrayal of relevant data, including, in some cases, alternative ways of obtaining the benefits sought in the research. Thus, the assessment presents both an opportunity and a responsibility to gather systematic and comprehensive information about proposed research. For the investigator, it is a means to examine whether the proposed research is properly designed. For a review committee, it is a method for determining whether the risks that will be presented to subjects are justified. For prospective subjects, the assessment will assist the determination whether or not to participate.
• The term "risk" refers to a possibility that harm may occur. However, when expressions such as "small risk" or "high risk" are used, they usually refer (often ambiguously) both to the chance (probability) of experiencing a harm and the severity (magnitude) of the envisioned harm.

Belmont Report
"benefit" is not a term that expresses probabilities

so-called risk/benefit assessments are concerned with the probabilities and magnitudes of possible harm and anticipated benefits

Belmont Report
The Systematic Assessment of Risks and Benefits

(i) Brutal or inhumane treatment of human subjects is never morally justified.

(ii) Risks should be reduced to those necessary to achieve the research objective. It should be determined whether it is in fact necessary to use human subjects at all. Risk can perhaps never be entirely eliminated, but it can often be reduced by careful attention to alternative procedures.

(iii) When research involves significant risk of serious impairment, review committees should be extraordinarily insistent on the justification of the risk (looking usually to the likelihood of benefit to the subject -- or, in some rare cases, to the manifest voluntariness of the participation).

(iv) When vulnerable populations are involved in research, the appropriateness of involving them should itself be demonstrated. A number of variables go into such judgments, including the nature and degree of risk, the condition of the particular population involved, and the nature and level of the anticipated benefits.

(v) Relevant risks and benefits must be thoroughly arrayed in documents and procedures used in the informed consent process.  

Belmont Report
Benificence thus requires that we protect against risk of harm to subjects and also that we be concerned about the loss of the substantial benefits that might be gained from research.
<table>
<thead>
<tr>
<th>Requirement</th>
<th>Explanation</th>
<th>Justifying Ethical Values</th>
<th>Expertise for Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social or scientific value</td>
<td>Evaluation of a treatment, intervention, or theory that will improve health and well-being or increase knowledge</td>
<td>Scarce resources and nonexploitation</td>
<td>Scientific knowledge; citizen’s understanding of social priorities</td>
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<tr>
<td>Scientific validity</td>
<td>Use of accepted scientific principles and methods, including statistical techniques, to produce reliable and valid data</td>
<td>Scarce resources and nonexploitation</td>
<td>Scientific and statistical knowledge; knowledge of condition and population to assess feasibility</td>
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<td>Fair subject selection</td>
<td>Selection of subjects so that stigmatized and vulnerable individuals are not targeted for risky research and the rich and socially powerful not favored for potentially beneficial research</td>
<td>Justice</td>
<td>Scientific knowledge; ethical and legal knowledge</td>
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<td>Favorable risk-benefit ratio</td>
<td>Minimization of risks; enhancement of potential benefits; risks to the subject are proportionate to the benefits to the subject and society</td>
<td>Nonmaleficence, beneficence, and nonexploitation</td>
<td>Scientific knowledge; citizen’s understanding of social values</td>
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<td>Independent review</td>
<td>Review of the design of the research, trial, its proposed subject population, and risk-benefit ratio by individuals unaffiliated with the research</td>
<td>Public accountability; minimizing influence of potential conflicts of interest</td>
<td>Intellectual, financial, and otherwise independent researchers; scientific and ethical knowledge</td>
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<td>Informed consent</td>
<td>Provision of information to subjects about purpose of the research, its procedures, potential risks, benefits, and alternatives, so that the individual understands the information and can make a voluntary decision whether to enroll and continue to participate</td>
<td>Respect for subject autonomy</td>
<td>Scientific knowledge; ethical and legal knowledge</td>
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<td>Respect for potential and enrolled subjects</td>
<td>Respect for subjects by (1) permitting withdrawal from the research; (2) protecting privacy through confidentiality; (3) informing subjects of newly discovered risks or benefits; (4) informing subjects of results of clinical research; (5) maintaining welfare of subjects</td>
<td>Respect for subject autonomy and welfare</td>
<td>Scientific knowledge; ethical and legal knowledge; knowledge of particular subject population</td>
</tr>
</tbody>
</table>

*Ethical requirements are listed in chronological order from conception of research to its formulation and implementation.*
<table>
<thead>
<tr>
<th>SECTION I: POTENTIAL BENEFITS</th>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Is there direct benefit to the subject?</td>
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<td>2. Does the research provide therapeutic benefit?</td>
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<td>3. Does the research primarily benefit society (involves procedures performed for research purposes only without direct benefit to subject)?</td>
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<td>4. Is compensation offered to the subject?</td>
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<td>5. Do the benefits of this research outweigh the risks?</td>
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Comments: