New IRB Member Orientation

Part IV: IRB Review Criteria
45 CFR 46.111 &
20 CFR 21.111

Criteria for IRB Approval

45 CFR 46.111 & 21 CFR 56.111

OHRE SOP 24.0

1. Risks minimized
2. Favorable risk : benefit ratio
3. Equitable selection of subjects
4. Informed consent sought
5. Informed consent documented
6. Monitoring plan for safety
7. Privacy and confidentiality protected
8. Additional safeguards for vulnerable populations

Levels of IRB Review

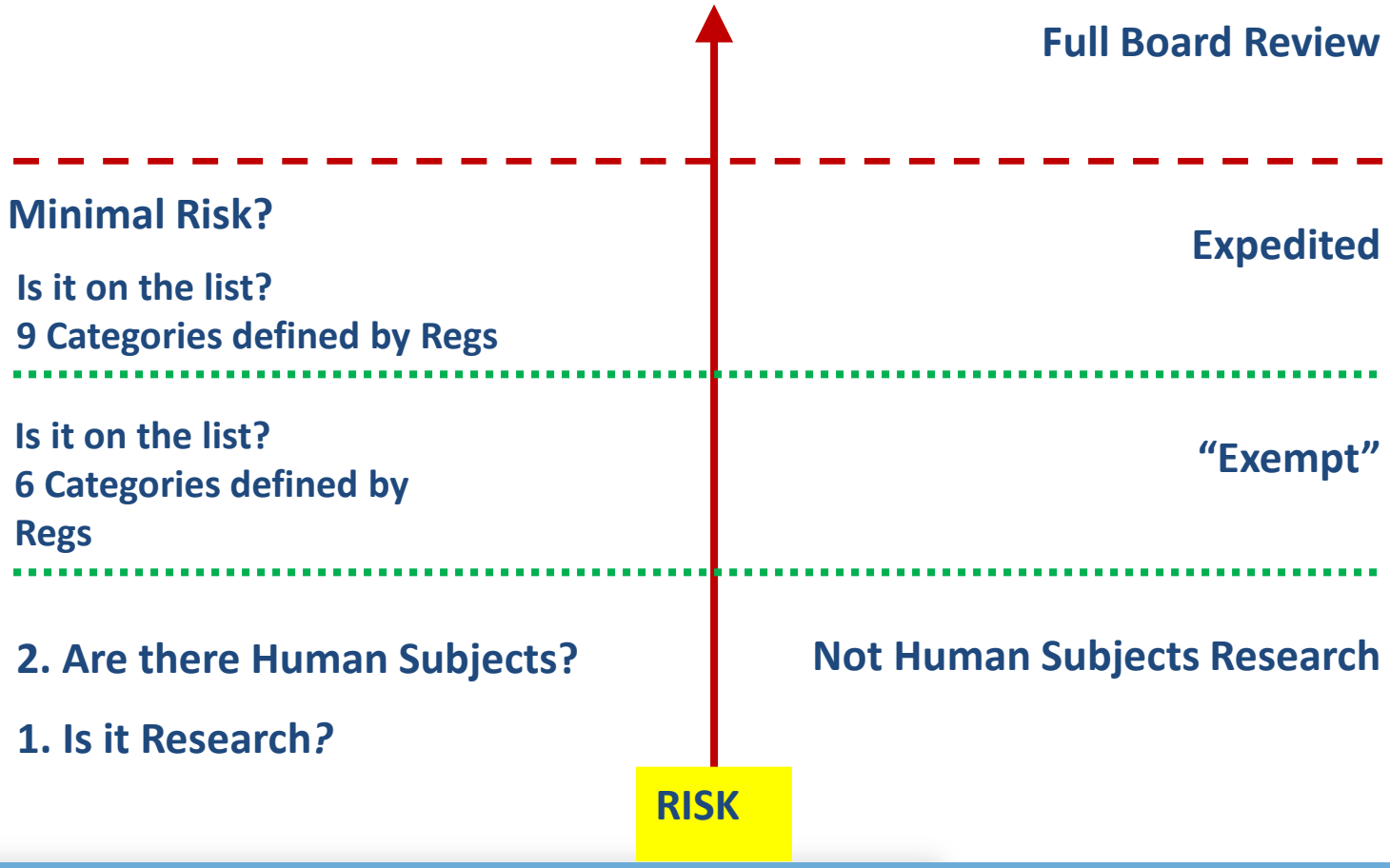
- **EXEMPT** – Applies to specific categories of research, most often with extremely low risk or anonymous data

- **EXPEDITED REVIEW** – Applies to specific categories of research with no more than minimal risk.

- **FULL COMMITTEE REVIEW** – All studies which do not qualify as exempt or expedited must be reviewed by a full IRB.

Note: ***The level of review is determined by IRB, not by the investigator or by the client. The requirements for each level are given in the regulations.***

Level of Risk Generally Determines Level of IRB Review



THE BELMONT REPORT

Ethical Principles and Guidelines for the Protection of Human Subjects of Research

Respect for Persons

Beneficence

Justice

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979

The Belmont Report

- **Respect for persons**: Informed consent
  - Individual autonomy
  - Protection of individuals with reduced autonomy
- **Beneficence**: Assessment of risks & benefits
  - Maximize benefits & minimize harms
- **Justice**: Selection of subjects
  - Equitable distribution of research costs & benefits

THE BELMONT REPORT: RESPECT FOR PERSONS

Respect for Persons

- People are autonomous
  - Reminder: UNC policy is no cold calls!
- Those with diminished capacity should be protected

Belmont & Informed Consent

- **Respect for persons**
  - Freedom to choose based on:
    - Information about the study
    - Comprehension
    - Voluntary

Informed Consent will….

……be sought from each prospective subject or their legally authorized representative

……be appropriately documented

46.116 & 117

Consent Is:

- A partnership contract with subject.
- The more the subject knows about a study, the better a resource they can be to the study.
- Is it possible for there to be a coercion-free consent process when they come to you in the white coat for a cure?
- Fear of dumb questions.
- Subjects may not know enough to know what to ask you—use leading questions.

When You Need an Adult Consent for a Pediatric Study.

- If your pediatric subject turns 18, then you need to re-consent the subject as an adult with an adult consent form.

- You must also remember to retain pediatric data until the pediatric subject becomes 21 &/or 6 years post study whichever is longer.

Data Retention Requirements

- **OHRP: 45 CFR 46.115: 3 years post study**
- **FDA: 21 CFR 56.115: 3 years post study**
  - **2 years following the date of marketing application approval for IND**
- **HIPAA: 6 years**
- **IRB Policy: 6 years or in case of pediatric research till child is 21.**

THE BELMONT REPORT: BENEFICENCE

The Belmont Report

- **Respect for persons**: Informed consent
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Beneficence in the Research Setting

1. Valid Study Design

2. Favorable Risk: Benefit

3. Competent Investigators

BELMONT REPORT: BENEFICENCE

Valid Study Design

Valid Study Design

- Will study design answer the research question?

- How does the IRB know?

Scientific Review

- Not the sole responsibility of the IRB
- Bad science = Bad ethics
- If not scientifically valid, how does one justify the risks?
- Regulations require IRBs to balance risk:benefit, which requires understanding of the science
- Consider clinical equipoise

Departmental Review

- Closest to the science of the research being proposed
- Know their researchers' skills & abilities
- Need to know what is being proposed
- Need to be represented on the IRBs

Department Approval

By approving, the Home or Administering department affirms that:

- The research is appropriate for the investigator and Department
- The investigator(s) are qualified to conduct the research
- There are adequate resources (financial, support, and facilities) available
- For units that have a local review committee for pre-IRB review, this requirement has been satisfied
- The department supports the application and its review by the IRB
- The department agrees to accept responsibility for managing data security risks in consultation with departmental or campus security personnel

Office of Human Research Protections (OHRP) Guidance on IRB Composition

(5)**Members Present at Convened IRB Meetings Lacked the Expertise to Make Determinations Required for Approval of Research**.

HHS regulations at 45 CFR 46.107(a) provide, among other things, that each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. In addition, the regulations provide that the IRB be sufficiently qualified through the experience and expertise of its members to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects and be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. **The convened IRB, when reviewing protocol applications, must have sufficient expertise among the members present at the meeting to make the determinations required for approval of research under HHS regulations at 45 CFR 46.111. We have determined that the members of the IRB present at convened meetings did not have the background and expertise necessary to review the research being proposed.**

http://www.hhs.gov/ohrp/compliance/findings/index.html#A3

What Does the IRB Receive to Judge the Study By?

Consider this Research Equation

Funding + IRB Approval = Study

Grant **Submission**

or

Garbage in/Garbage Out

BELMONT REPORT: BENEFICENCE

Risk:Benefit Ratio

Risk Benefit Ratio

Risk/Benefit Ratio

"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.

Institutional Review Board Guidebook, 1993

Risk/Benefit Ratio

"In evaluating risks and benefits, the IRB should consider only those risks & benefits that may result from the research (as distinguished from risks & benefits of therapies subjects would receive even if not participating in the research."

45 CFR 46.111.a.2

Risk

"The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal regulations define only 'minimal risk'. "

Institutional Review Board Guidebook, 1993

Minimal Risk

"A risk is minimal where the probability & magnitude or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests."

Institutional Review Board Guidebook, 1993

45 CFR 46.101.b.2.I & ii

ii any disclosure of the human subjects' responses outside the research could **reasonably** place the subjects at risk of **criminal** or **civil liability** or be damaging to the subjects' **financial standing**, **employability**, or **reputation**."

Types of Risk

- **Physical** (e.g. pain, drug side effects, or injury)
- **Psychological** (e.g. emotional distress)
- **Social** (e.g. stigmatization)
- **Economic** (e.g. loss of job—breach of confidentiality that relates to stigma, or workplace competency issues)
- **Legal** (requirements to report some illegal activities, whether the focus of the study, or which emerge without prompting)

THE BELMONT REPORT: JUSTICE

Belmont's Justice

1. Blend of Judeo-Christian tradition of protection of widows and orphans

2. Marxist dictum "from each according to ability; to each according to need"

3. Seen in subject selection.

Justice as Seen in Research Studies

- Unbiased Subject Selection
- Fair Recruitment

BELMONT REPORT: JUSTICE

Unbiased Subject Selection

Unbiased Subject Selection

From Belmont:

- To each person according to societal contribution,
- To each person according to merit.”

Vulnerable Populations

Are they needed to answer the research question?

- Pregnant Women, Human Fetuses & Neonates: Subpart B
- Prisoners: Subpart C
- Children: Subpart D
- Diminished Capacity *coming……*

Special Populations

- ✓ The federal regulations require that IRBs give special consideration to protecting the welfare of particularly vulnerable populations, persons who may not be able to make decisions for themselves or who may be unduly influenced by others in their decisions.
- ✓ There are specific regulations that must be followed to include children, prisoners, pregnant women (because of the need to protect the unborn child) in research.
- ✓ Other populations, such as mentally disabled persons, the homeless, or those who are economically or educationally disadvantaged, may also need special protection.

BELMONT REPORT: JUSTICE

Fair Recruitment

Subject Selection

- Selection of subjects is equitable

- Think Belmont Principles # 1 & 3—

  Respect for persons

  Justice

"Sometimes, with the best of intentions, scientists and public officials… working for the benefit of us all, forget that people are people. They concentrate so totally on plans and programs, experiments, statistics- on abstractions- that people become objects, symbols on paper, figures in a mathematical formula…"

Atlanta Constitution, July 27, 1972

Obtaining Consent

- Obtaining consent is a PROCESS in which...
  - investigator discloses all relevant information
  - potential subject has opportunity to ask questions
  - investigator answers questions
  - subject signs a consent form

- The consent form is a permanent record of...
  - information conveyed
  - subject's willingness to participate

Consent Is:

- Partnership contract with subject
- More the subject knows about study, the better resource they can be for your study

Written Consent Forms

- Required elements are covered in templates generated by the on-line application
- Language must be understandable to subject or representative
- Some elements, including signatures, may be waived under certain circumstances

45 CFR 46.116, 21 CFR 50.25

Required Elements of Consent

- Study involves research
- Purpose
- Duration of the subject's participation
- Description of the procedures
- Foreseeable risks and discomforts
- Reasonably expected benefits to subject or others

45 CFR 46.116, 21 CFR 50.25

Required Elements of Consent

- Alternatives, if any
- Confidentiality
- Compensation for injury (> minimal risk)?
- Contacts for questions about the research, research-related injury, subjects' rights
- Voluntary participation, refusal without loss of benefits, withdraw at any time

45 CFR 46.116, 21 CFR 50.25

Prisoners

"The definition of minimal risk for research involving prisoners differs somewhat from that given for non-institutionalized adults. "

Institutional Review Board Guidebook, 1993

Prisoners: Minimal Risk

"Risk of physical or psychological harm that is no greater in probability & severity than that ordinarily encountered in the daily lives, or in the routine medical, dental or psychological examinations of healthy persons.."

Benefit

- “A valued or desired outcome; an advantage.”
- Does **NOT** include any reimbursement or remuneration given to subjects

Risk Assessment

- Risks to subjects are minimized
- Risks to subjects are reasonable in relation to anticipated benefits
- Remember Belmont Principle #2:

Beneficence

Beneficence

- **Respect** for their decisions
- **Protection** from harm
- In Belmont beneficence is an ***obligation,*** not just an act of kindness. Thus,
  - *Do not harm*
  - *Maximize benefits & minimize potential harm*

Safety of Subjects

- "When appropriate, the research plan makes adequate provision for monitoring the data collection to ensure the safety of subjects."

- Not just DSMBs

Privacy

- “When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.”
- Can’t just say it will be done, show me