Defining Roles, Expectations, and Challenges for the Non-Scientist IRB Member

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Disclosure: Michelle Feige, Dahron Johnson, Nancy Olson

We have no relevant personal/professional/financial relationship(s) with respect to this educational activity

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Learning Objectives

1. Describe the background, the role and expectations of the non-scientist
2. Define research terminology that commonly occurs during protocol review
3. Provide tips for the non-scientist when reviewing research
4. Provide suggestions for success

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The Importance of Your Role

- Regulatory perspective
- From your perspective…
  - Your value
  - Your importance
  - Your role
  - Your reflections

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The Fundamentals: The Belmont Report

- Respect for Persons- informed consent
- Beneficence- risks and benefits
- Justice- selection of subjects

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IRB Membership Requirements

- Number of Members
  - minimum of 5 members - §46.107(a)
- Experience and Expertise - §46.107(a)
- Diversity of Members - §46.107(a) & (b)
  - At least one:
    - scientist - §46.107(c)
    - nonscientist - §46.107(c)
    - nonaffiliated - §46.107(d)
- Prisoner Representative - §46.304(b)

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Scientist & Nonscientist

- Minimum one nonscientist and one scientist
- "Nonscientist" must be present

Considerations

- training
- background
- occupation

Defined by what you are NOT vs. what you ARE! What qualities SHOULD the non-scientist have???

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Expectations: SCIENTISTS

Understanding of:

- Substantive area
- Study question/hypothesis
- Research design
- Risk/benefit
- Standard of care
  - Risks
  - Costs
- Consent form(s)

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Expectations: NON-SCIENTISTS

Understanding of:

- **General research principles**
- **Research idea(s)**
- **Appreciation of risk vs. benefit tradeoff**
- **Patient/participant/community(?) perspective**
- **Consent form(s)**
  - **Readability/translation**
- **Costs**

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Your Role?

The good news and the bad news

Non-scientist IRB member responses - Main Roles

- 72% -main role of non-scientist IRB members is to review and make recommendations about the informed consent document
- 92% felt they made other important contributions
- 66% answered that they sometimes or often asked questions about the scientific design of protocols
- 84% answered they sometimes or often asked about the informed consent.
- 44% reported they often ask questions concerning the protection of human subjects that are unrelated to the informed consent document

IRB. 2008 Sep–Oct; 30(5): 8–13.,Roles and Experiences of Non-scientist Institutional Review Board Members at the National Institutes of Health, Robert D. Allison, Lura J. Abbott, and Alison Wichman

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- 88% occasionally had been intimidated and felt disrespected
- 47% identified lack of education and training as a problem
- 78% wanted more intensive education and training for future non-scientist/nonaffiliated members

Acad Med. 2003 Feb;78(2):212-8. The roles and experiences of nonaffiliated and non-scientist members of institutional review boards. Sengupta, Lo B.

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IRB = Working Together

- It's not just about the Informed Consent!
- **General Research "jargon" and principles**
  - **Broad types of studies and goals**
  - **Validity**
  - **Sample size**
  - **Interim analysis**
  - **Privacy**
  - **Data security**
- **Consent Form Readability**
- **Costs**
- **Compensation**

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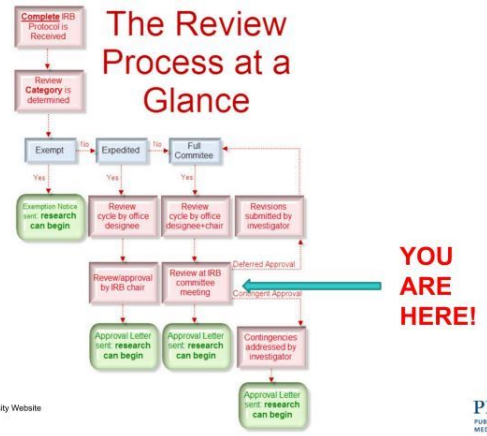
The IRB Review Process and YOU!



The Review Process at a Glance

YOU ARE HERE!

Image from San Francisco State University Website

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Your Job: Reviewing Criteria for IRB Approval… Findings under §46.111

- **Risks minimized**
  - Alternative/fewer procedures?
  - Sound research design
- **Risk/benefit ratio reasonable**
  - alternative ways of obtaining info?
  - Are risks justified?
  - Assessment of ratio will inform subject's determination of participation
- **Subject selection equitable**
  - Consider purposes and setting of research
  - Not systematically included or excluded unless scientific rationale

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Criteria for IRB Approval, cont'd Findings under §46.111

- **Informed consent** – obtained & documented (unless waived)
  - Best method? Information, comprehension, voluntariness
- **Data monitored** (when appropriate)
  - To ensure safety
- **Privacy and confidentiality** (when appropriate)
  - Adequate provisions; not always possible
- **Safeguards for vulnerable subjects**
  - Options? 3rd party monitor?

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Informed Consent

Key principles of the informed consent process:

- **Full disclosure of the nature of the research and the subject's participation**
- **Adequate comprehension on the part of the potential subjects or legally authorized representative (LAR)**
- **The subject's voluntary choice to participate or not**
  - **Minimize the possibility of coercion or undue influence.**

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Basic Elements of Informed Consent

- **Research**
  - **- purpose**
  - **- duration**
  - **- procedures**
- **Risks, discomforts**
- **Benefits**
- **Alternatives**
- **Confidentiality**
- **Compensation for injury**
- **Whom to contact**
- **Right to refuse, withdraw without penalty**

§46.116(a)

Note: Additional elements, when appropriate

§46.116(b)

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Revised Rule Changes in IC

Additional Elements of Informed Consent 46.116(c)

- 46.116(c)(7) requires a statement that biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit.
- 46.116(c)(8) requires a statement about whether clinically relevant research results, including individual research results, will be disclosed to subjects. This provision is intended to pertain to all clinically relevant research results, including general or aggregate research findings and individual research results.
- 46.116(c)(9) requires a statement about whether the research project might include whole genome sequencing (the sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen)

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Potential Review Challenges

- Compensation
- Randomized Controlled Study
- Placebo Controlled Study
- Phase 1 Drug Study
- Social/Behavioral Research

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Compensation

The HHS regulations require that "An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence" (45 CFR 46.116).

- **How much $$$?**
- **For what?**
  - **time**
  - **inconvenience**
  - **discomfort**
  - **other considerations**
- **Should be just and fair**
  - **the study population**
  - **context of the research**
- **Have SOPs!**
- **Terms of payment**
- **Partial or no payment (e.g., withdraws or removed from study) Paid when?**
- **Payment be prorated**

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Randomized Controlled Study

What is a randomized controlled study?

- Participants are randomized to receive one of at least two therapies, e.g., experimental therapy or conventional therapy.
  - Often used to test and compare effectiveness

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Randomized Controlled Study

- **Things to consider:**
  - Some may receive a therapy that is not the best available
  - Is one of the therapies usual care? If not, why not?
  - Is there sufficient information to support the scientific question?
    - Prior clinical findings
    - Efficacy of current standard
  - Is data safety monitoring appropriate? DSMP/DSMB
  - Does the consent document adequately describe randomization, risks and benefits?

Steven Joffe & Robert Troug, Equipose & Randomization, Ezekiel Emanuel, Reidar,Lie, et al, (eds.). *Oxford Textbook of Clinical Research Ethics* (New York: Oxford University Press, 2008), 245-260.

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Placebo Controlled Study

What is a placebo controlled study?

- A type of randomized controlled study, but one of the arms is a placebo
  - "gold standard" for study design

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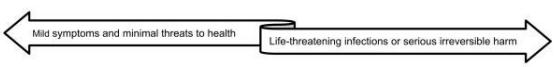
Placebo Controlled Study

- **Potential issue:**
  - Some participants will receive no therapy/may be denied a medical benefit
- **Things to consider:**
  - Does the placebo expose participants to unnecessary risks?



  - Does the consent document adequately describe the risks and burdens of being in the placebo group?

Dunn C, Chadwick G, Special Ethical Concerns in Clinical Research. *Protecting Study Volunteers in Research* (Centerwatch, 3ed), 129-133.

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Drug Studies

Normally done in three phases – each phase exposes more people to the drug

- Phase 1
  - Phase I drug studies try to show that a new drug can safely be used in people
- Phase 2
  - Phase II drug studies collect more information about drug safety and look at how well/if the new drug works
- Phase 3
  - Phase III drug studies compare the new drug to current care, to find out if the new drug is better than current and/or causes fewer side effects.

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Phase 1 Drug Studies

Groups of participants are administered increasing dose of experimental drug(s) to find the maximum dose that is safe to give, ie the dose that works best without causing severe side effects

- **Things to consider:**
  - First-in-human or first-in-population?
  - Starting dose?
  - Therapeutic misconception for non healthy individuals
    - Phase 1 studies are not designed to test how well a drug works
  - Does the background section refer to prior studies as a basis for defining the starting dose?
  - Ensure that the consent document does not misrepresent to non-healthy individuals that they will receive a therapeutic dose
  - When enrolling non-healthy individuals, consider whether a delay in providing other routine care is a risk.

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Social/Behavioral/Education Research (SBER)

What is SBER?

- Applies behavioral and social sciences to research questions
  - Seeks to improve our understanding of relationships and interactions between and among individuals and groups
  - Examines human behavior, attitudes, beliefs and interactions, as well as social, educational and economic systems, organization and institutions
- Uses interviews, surveys, focus groups, educational practices, observation, and/or behavioral manipulations

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SBER

- **The research may be asking questions about a sensitive topic with a vulnerable population**
  - Drug abuse among teenagers
  - Domestic violence with known offenders or victims
  - Employees being asked about employers
- **Things to consider:**
  - How will privacy be protected?
    - Think about study population, recruitment, consent process, data collection/study procedures
  - How will confidentiality be protected?
    - May need greater protections for sensitive information
  - The nature of the risks and harms
  - Are there factors likely to contribute to increased risk in relatively low-risk research?
  - Are there procedures in place in case someone needs assistance?
  - Are there referrals or emergency numbers provided in case of problems/questions after participation is complete?

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Review challenges can be found anywhere

- In protocol inclusion criteria
  - "The Children's Heart Center Tissue Repository"
    Included parents, siblings and all second-degree relatives
  - Randomized, double-blind drug study with a 6 week washout period
    Included patients currently stable on medication
- Drug study with depression scale questionnaire
  - Mental health professional involved?
  - Plan of action if suicide ideation identified?
- Device study
  - Participants are told they can withdraw and have device removed
    - Who will cover the cost to remove?
    - What if some pieces of the device will have to remain?
- Regulations require reporting unanticipated problems involving risks to subjects or others.
  - Consider risks to others during review?

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Suggestions for Success

- Familiarize yourself with the study topic (Google is your friend)
- Think critically and be skeptical
- Ask questions that seem "obvious" – others most likely have the same question (even the scientists)
  - Reach out to the Chair, IRB staff, and the Primary reviewer prior to the meeting to go over your questions
- Write down your comments and reference points in protocol/informed consent form
- Don't be afraid to develop a "niche"

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Why anyone would want to fill: The community member role?

Positive Role Associations:

+Feeling Needed

+Contributions of Value (even when being corrected)

+Altruism/Pride representing general/specific communities

Project for Critical Imagination

How to Enhance Community Member's Sense of:

+Being Valued

+Having Legitimate Voice

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Listening with Both Ears

"But human excellence grows like a vine tree, fed by the green dew, raised up, among wise men and just, to the liquid sky."
Pindar, *Nemean* VIII 40-2

- *To Remain Attentive to My Communities (However Defined)*
- To Carry Information, Issues Back to (My) Communities from Research
- *To Hear Concerns, Issues of Research Community*
- To Convey Questions, Concerns of (My) Communities to Research Side

Project for Critical Imagination

Creating, Supporting Connections between Research and Communities in Which Research Takes Place
+(Note to Institution: I'm here; utilize me!)

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Community: Towards a Personal Understanding




1) ***How have your communities shaped "community" for you?***
2) ***One's definition of "community" shapes (inter)action with/in them.***
3) ***Community is always plural: remain conscious of which are at play.***
4) ***On communities' varying "rationalities:" what logic(s) are at work?***

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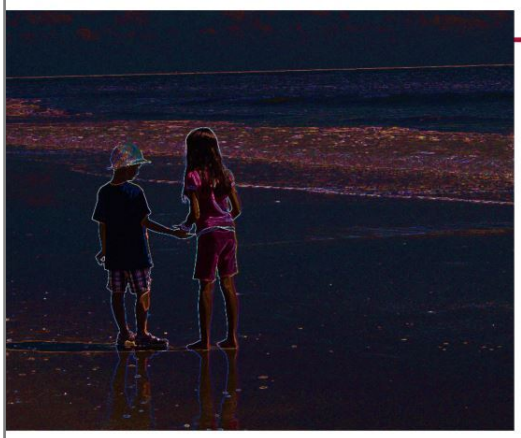
Mutual Projects of Critical Imagination



- *Working together to sort out ways to move forward*

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Articles of Interest

- E Kodish, et al., Ethical Issues in Phase I Oncology Research: A Comparison of Investigators and Institutional Review Board Chairpersons, *Journal of Clinical Oncology*, Vol 10, No 11 (November), 1992: pp 1810-1816
- R Allison, et al., Roles and Experiences of Non-scientist Institutional Review Board Members at the National Institutes of Health, *IRB*. 2008: 30(5): 8-13.
- R Amdur and E Bankert, Institutional Review Board Member Handbook, 3rd ed, 2011.
- U.S Department of Health and Human Services, Food and Drug Administration, Center for Devices and Radiological Health (CDRH), Information Sheet Guidance for IRBs, Clinical Investigators and Sponsors, Significant Risk and Nonsignificant Risk Medical Device Studies
- L Rubinstein and R Simon, Phase I Clinical Trial Design, in Budman, Calvert, Rowinsky, (eds.), *Handbook of Anticancer Drug Development*, Elsevier, Amsterdam, 297-308, 2003.
- F Miller and C Grady, The Ethical Challenge of Infection-Inducing Challenge Experiments, *CID*, (October) 2001:33

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Questions?

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