International Research: Applying Ethical Principles and Research Guidelines in Global Settings

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Welcome

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International Research: Applying Ethical Principles and Research Guidelines in Global Settings

A 90-minute interactive webinar

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Issues to Consider for IRBs that Review International Research Involving Vulnerable Populations

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Overview

- FWA Considerations
- Regulatory expectations for IRBs
- Scenarios where regulations are difficult to export

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What does your FWA say?

- **If a U.S. institution:**
  - **Ethical standards = Belmont**
  - **Procedural standards = Common Rule**
- **What if a non-US institution?**

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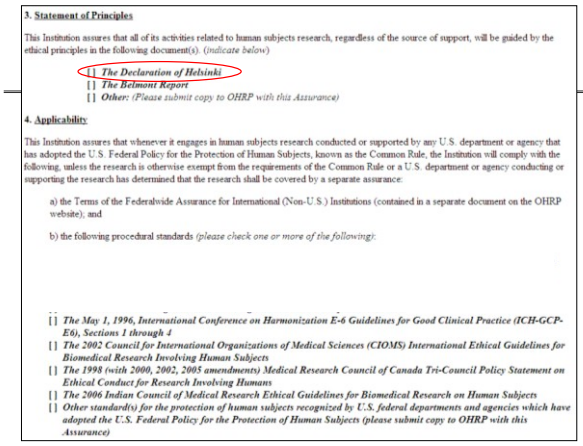

3. Statement of Principles

This Institution assures that all of its activities related to human subjects research, regardless of the source of support, will be guided by the ethical principles in the following document(s). *(indicate below)*

[ ] ***The Declaration of Helsinki***
[ ] ***The Belmont Report***
[ ] ***Other:*** *(Please submit copy to OHRP with this Assurance)*

4. Applicability

This Institution assures that whenever it engages in human subjects research conducted or supported by any U.S. department or agency that has adopted the U.S. Federal Policy for the Protection of Human Subjects, known as the Common Rule, the Institution will comply with the following, unless the research is otherwise exempt from the requirements of the Common Rule or a U.S. department or agency conducting or supporting the research has determined that the research shall be covered by a separate assurance:

a) the Terms of the Federalwide Assurance for International (Non-U.S.) Institutions (contained in a separate document on the OHRP website); and

b) the following procedural standards *(please check one or more of the following)*:

[ ] ***The May 1, 1996, International Conference on Harmonization E-6 Guidelines for Good Clinical Practice (ICH-GCP-E6), Sections 1 through 4***
[ ] ***The 2002 Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines for Biomedical Research Involving Human Subjects***
[ ] ***The 1998 (with 2000, 2002, 2005 amendments) Medical Research Council of Canada Tri-Council Policy Statement on Ethical Conduct for Research Involving Humans***
[ ] ***The 2006 Indian Council of Medical Research Ethical Guidelines for Biomedical Research on Human Subjects***
[ ] ***Other standard(s) for the protection of human subjects recognized by U.S. federal departments and agencies which have adopted the U.S. Federal Policy for the Protection of Human Subjects (please submit copy to OHRP with this Assurance)***

Is there really a choice?

Federal Register Notice
"Interpretation of Assurance Requirements"

"Some regulated institutions may have been confused by the fact that several … procedural standards are listed on the FWA form for … non-U.S. institutions…"

(FR: July 7, 2006 Volume 71, Number 130)

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Interpretation of Assurance Requirements

"…and interpreted this to mean that non-U.S. institutions have a choice of whether or not the requirements of 45 CFR part 46 must be met for HHS conducted or -supported research conducted at their institutions."

"Such an interpretation would be erroneous."

(FR: July 7, 2006 Volume 71, Number 130)

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Interpretation of Assurance Requirements

*"For HHS-conducted or -supported research, all institutions holding an … FWA … must comply with the requirements of 45 CFR part 46. That **compliance is required regardless of whether the institution marked … other procedural standards** on the FWA form… ."*

(FR: July 7, 2006 Volume 71, Number 130)

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Why is this a problem?

- The local IRB may not have made required regulatory determinations
- IRB roster may not include members required by Common Rule
- Continuing review may not occur with frequency required by Common Rule
- Protections for special populations may not contain specific sub-part requirements

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When relying on a local IRB

- Communicate with local IRBs
- Determine what standards were applied in review of research – ask specific questions
- Be clear in IRB records what portion of local review you are relying on
- Maintain complete documentation

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Expectations for IRBs from the Belmont Report and the Common Rule when Reviewing Research on Vulnerable Populations

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Belmont

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.

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Approval Criteria (45 CFR 45.111(a)(3))

Selection of subjects is equitable…. the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be should be particularly cognizant of the special problems of research involving vulnerable populations….

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IRB Membership (45 CFR 46.107(a))

If an IRB regularly reviews research that involves a vulnerable category of subjects, such as …. consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

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Meeting Expectations

- **Identify an expert with relevant background and experience**
  - **PRIM&R International Members**
  - **Fogarty-supported Bioethics Program Trainees**
- **Obtain an opinion from an experienced member of the site IRB**
- **Require site IRB approval first**

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Meeting Expectations

- Create a supplement to your IRB application
  - Design the questions to address issues commonly raised by the IRB
- Require PI participation in IRB meetings
- Require more rigorous/frequent monitoring

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Other Resources

- NBAC report on international research
- CIOMS and other international guidelines
- OHRP's International Activities Program
- FIC International Research Ethics Resources
- NGOs that work with the population/in region

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Common Scenarios that Challenge US IRBs when Reviewing International Research

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Informed Consent

- International application of Western informed consent standards
  - Different beliefs about autonomy
    - Role of elders / community leaders / head of household
  - Translation issues
  - Documentation issues
    - Mistrust of signing papers
    - Illiteracy

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Research with Children

- Research with Minors
  - Local definitions of minor; guardian
  - Parental permission requirements
  - Research with orphans and vulnerable children
- Identify the issues in advance and proactively address them. Document findings!

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Local Laws

- Absence of regulation / policy regarding research (and limited or no enforcement)
- Common practice versus legal requirements in the provision of healthcare
- Multi-national research = multiple local norms

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Maintain Appropriate Documentation

- Credible sources – official email / letterhead
- Joe_PI@yahoo.com may not be best resource!
- Written correspondence rather than verbal assurance
- If in doubt, seek second opinion / obtain additional confirmation
- Maintain good documentation

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Toward valid and respectful Informed Consent in Resource Poor Countries

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Assumptions

- Experienced audience
- Familiar with informed consent generally
- Interested in how experience with informed consent can be applied internationally

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Elements of informed consent

- Disclosure of Information
- Understanding
- Voluntary Authorization
- Competence

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Disclosure – additional considerations

- **Think** more **broadly** about **when, how, to whom** to disclose
  - **Community or group introduction of study (first)**
    - Street theater
    - Radio announcements
    - Group discussions
    - Community liaisons
    - Involvement of family members/others
  - **Individual disclosure and discussion (later)**
    - More pictures and props

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Disclosure – additional considerations

- **Background work (Rapid Ethnographic Assessment)**
  - Helps identify the best strategies for target population
  - Helps ensure messages are appropriate, clear, sensible to target audiences

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Understanding – additional considerations

- May be limited familiarity with research
  - Doctor admitting uncertainty is problematic
- Usual procedures may be misunderstood
  - Blood drawing
  - Signing of forms
  - "We fill in the narratives we don't understand"

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Understanding – additional considerations

- No word for "research" or "placebo" or "privacy"
  - Explanations can be lengthy
  - Explanations can be inaccurate!!
- No standards re: translation quality (back translation helps)

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Assessing understanding becomes important

- Most investigators do not assess understanding (Tomamichel 1995; Kass 2005)
  - 65% investigators thought assessing understanding was important
  - 16% of them did so

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Helpful strategies

Ethnographic work to guide and improve disclosure
When, how, to whom
Wording, analogies that make sense

Emphasize key concepts (?)
What are 5 most important things to understand?
Explain WHY key procedures are done (not just HOW)

Assessment of understanding
Quizzes pretty good ("corrected feedback")
Best (?) may be verbalization of key concepts (simple!!)

Community discussions DURING project also

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Project staff (in country) comments about enrollment/voluntariness

"What if we really believe it is the best thing for them to be in the study?"

"If we don't enroll enough people the study/we will be in trouble."

"If she changes her mind, you try to convince her otherwise."

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Informed Consent- Concluding messages

Ethnographic work: beliefs about disease, about research, how concepts are described

"**Menu of methods**" for informing

Listen to local people — their ideas re: informing, communicating, checking understanding

Question/answer to check understanding

What is most important? Certain aspects of research will be misunderstood: try to anticipate and be creative; determine which are essential

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Informed consent: concluding messages

Respect both/multiple traditions for informing and decision-making, if possible

Training for "**on the ground**" staff essential
Informed consent is "necessary but not sufficient" for an ethical study; participants still expect (and deserve) protection

Think beyond the consent form!!!

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Considering Beneficence in International Research

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Beneficence

- Minimizing risk of harm
  - individual vs group harms
  - physical/psychological vs social harms
- Maximizing benefits
  - individual vs community
  - extent of researchers obligations

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Minimizing risk

- Individual level harms
  - physical/psychological
  - social harms
- Group/community level harm
  - what are the research associated risks?
  - are there measures to minimize risk?

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Scenario – HIV Transmission in a Border Area

- Long haul truck drivers from Country A travel routes through Country B. A study aims to determine the prevalence of HIV in the truckers.
- Truckers from Country A are not well-regarded in Country B. In addition, there is a high level of stigma associated with HIV.

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Mitigating Group Risk

- Demonstrating a link between truckers from Country A and HIV infection may generate hostility towards the truckers.
- Can study results be disseminated in a way that is sensitive to these tensions?
- Can other risks be anticipated?

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Maximizing Benefits

- Individual level
  - Only those related to the research?
  - Extra, or ancillary, benefits provided?
- Extension of benefits to the community
  - Do the researchers have an obligation to the community?
  - Where can a reasonable line be drawn?

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Scenario: Ancillary Care

- A clinical research site is located in an area that is under-served by the public health infrastructure.
- Study participants have started asking the researchers to treat their children for intestinal parasites.

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Issues

- Are there constraints that would prevent researchers from providing treatment?
  - Restrictions on use of funds
  - Lack of staff w/ appropriate expertise
- Where do these obligations end?
  - Treatment for chronic conditions
  - Transportation to another facility

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Scenario: Community Benefit

- A research study is proposed in an area with limited laboratory capacity.
- The site is demanding that the study team build a laboratory onsite, train local staff, etc. as a condition for bringing in the study. Rationale is that this will benefit the community long-term.

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Issues

- Is this a fair demand?
  - Do researchers have an obligation to improve the settings where they will conduct research?
- Does this create a slippery slope for choosing research sites?
  - Could this lead to "bidding" on research?

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Managing Benefits Issues

- Ask researchers about anticipated benefit issues.
- Consider impact of the research beyond the individual participant.
- Ask the study team how it will manage anticipated situations.

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Justice and International Research

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Justice

General Definition: fairness

Distributive justice: a *fair* distribution of benefits and burdens.
Leads to questions of why that population was chosen for the research.
Leads to questions of whether, during or after research studies, study populations get their "fair share."

Historically - Justice requirement is responsive to concerns about exploiting a given population due to disadvantage or convenience.

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What increases likelihood of exploitation? (UNAIDS)

Less experience with scientific research

Less local infrastructure for health care and treatment

Less ability to give voluntary informed consent, due to social, gender, class inequities

Less experience or capacity with scientific and/or ethical review

Less infrastructure to conduct own research

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Research and justice: where do they intersect?

Research Agenda writ large:
How are global research dollars distributed--10/90 gap

How is population selected for *this study?*
Are communities over used or under used?
Is study question relevant to them?

What is provided during studies to participants?
Control group interventions
Ancillary care provisions

What do communities get out of this longer term?
What is owed after a study, prior agreements
"Indirect benefits"- training, clinics, labs, jobs, materials

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What do CIOMS guidelines say related to justice?

Must be responsive to health needs of host country (prevalence not enough)

Disease is important problem in host country

Agree in advance that products will be made reasonably available afterward

Develop capacity to carry out similar projects independently, including ethical review

Obligations clarified in advance

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Ancillary Care challenges

Ancillary Care - additional care participants might need that are unrelated to the study itself

Belsky/Richardson: What dictates duties?

- Vulnerability of population
- Depth of Relationship
- Degree of gratitude toward population
- Degree of dependence
- (Also relevant- importance of reasons against, e.g., cost, personnel required, threats to validity)

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What is the role of the IRB in achieving justice?

Clear

- Why this population? Scientific justification?
- Relevant for subpopulations WITHIN countries, too
- Ancillary care—Easy to provide and/or directly related

Murky

- Ancillary care that is more difficult
- Dissemination as IRB requirement
- Asking about Future access to intervention

Not current standard

- Global research agenda
- Future access required as a condition for approval
- More generalized ancillary care

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Questions and Comments

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at the top of the screen.

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Thank you for joining us!

Joan Rachlin, JD, MPH
Executive Director

Please complete the evaluation.

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