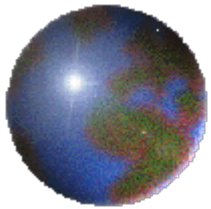


What Makes International Research Ethical (Or Unethical)?

Eric M. Meslin, Ph.D
Indiana University Center for Bioethics

Why Should We Care?

- Volume of health research is increasing
  - more researchers, more collaborations, more research subjects, more money
  - more opportunity to benefit (and harm) persons as well as international relations between institutions and countries
  - More involvement of pharmaceutical companies
- Inequity in research in developing countries remains
  - 10/90 gap: only 10% of all research money is being spent on diseases that affect 90% of the world's people
- Controversial studies are being reported
  - Placebo-controlled perinatal HIV transmission studies
  - Collection of genetic samples in China without consent
- Increasing concern about the "export" of U.S. regulations
  - Increasingly seen as 'paternalistic
- Research is becoming a topic of interest beyond health circles
  - Economic development, Trade policy, National Security

What Does It Mean to Say That Something (Someone) Is Ethical (Or Unethical)?

- Traditional moral theory often distinguishes between
  - Actions or behaviors (e.g., ends, rules)
  - Character of the actor (e.g., traits, virtues)
- Bioethics often adds additional components
  - Procedures (e.g., fair process)
  - Satisfaction of certain principles, standards
- Neither approach is completely satisfactory
  - The problem of universalizability
  - The problem of incommensurability

What Should We Ask?

- Why are we going there?
  - Justification
- How will we behave when we are there?
  - Conduct of the study
- What will we do when we leave?
  - Post-trial benefits

What Makes Clinical Research in Developing Countries Ethical?

- Principles
  - Collaborative partnership
  - Social value
  - Scientific validity
  - Fair selection of study population
  - Favorable risk-benefit ratio
  - Independent review
  - Informed consent
  - Respect for recruited participants and study communities

    – Emanuel, et al, *Journal of infectious Diseases* (2004)

From Principles to Benchmarks

- Principle: Collaborative Partnership
  - Benchmarks:
    - Develop partnership
    - Share responsibilities for determining problem, assessing value, planning, conducting, oversight, integration
    - Respect community values, culture, tradition, social practices
    - Develop capacity to become true partners
    - Ensure that participants benefit from research
    - Share fairly the financial and other rewards

From Benchmarks to Implementation

- Benchmark: Respect community values, culture, tradition, social practices
  - Implementation issues:
    - Meaning:
      - What does “should respect” mean? Is it like “should consider”?
      - And if so, does it mean: “be mindful of”, “be aware of”, “be sensitive to”, (which are desirable practices that may contribute to productive collaboration)
      - Or does it mean : “should adopt where possible”, “should make reference to”, or “should rely on”? (which may result in disagreement)
    - Resolving disagreements
      - Difficult to compromise on traditions (social norms and practices)
      - Who decides?

From Benchmarks to Implementation

- Benchmark: Ensure that participants benefit from research
  - Implementation issues:
    - Meaning:
      - What does “benefit” mean?
        - Drug? Roads? Infrastructure?
      - Limited to trial participants? What about communities?
      - On whose shoulders does any obligation to provide benefit fall?

From Principles to Benchmarks

- Principle: Informed Consent
  - Benchmarks:
    - Involve the community in establishing recruitment procedures and incentives
    - Disclose information in culturally and linguistically formats
    - Implement supplementary community and familial consent procedures where culturally appropriate
    - Obtain consent in culturally and linguistically formats
    - Ensure freedom to refuse or withdraw

From Benchmarks to Implementation

- Benchmark: Obtain consent in culturally and linguistically formats
  - Implementation Issues:
    - Western legal tradition as the origin of the concept is not universal
    - Federal regulations specify written consent with exceptions; in many countries the reverse is true
    - Consent involving men and women differ
    - Therapeutic misconception

Solutions

- Top Down
  - Harmonization of rules, regulations
  - Regulatory reform
- Bottom Up
  - Prior agreements
  - Capacity building

Top Down:
Harmonization of Guidelines

- CIOMS
- Council of Europe
- Declaration of Helsinki
- International Conference on Harmonization
- UNAIDS
- UNESCO Declaration on the Human Genome
- WHO Operational Guidelines
- European Privacy Directive

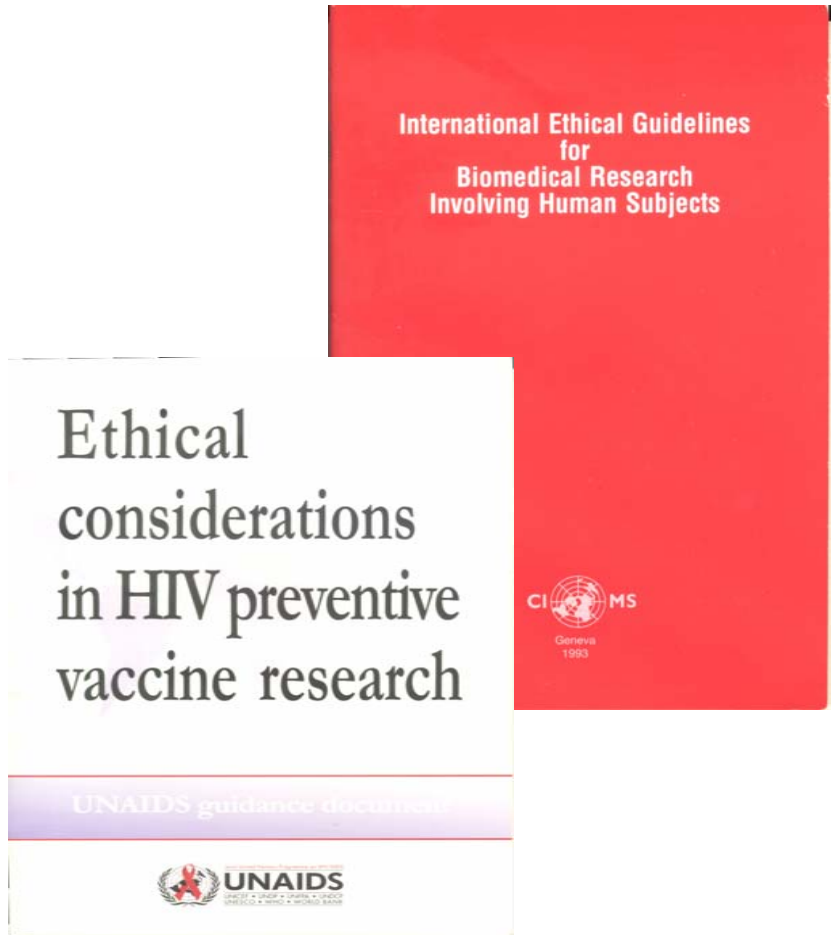
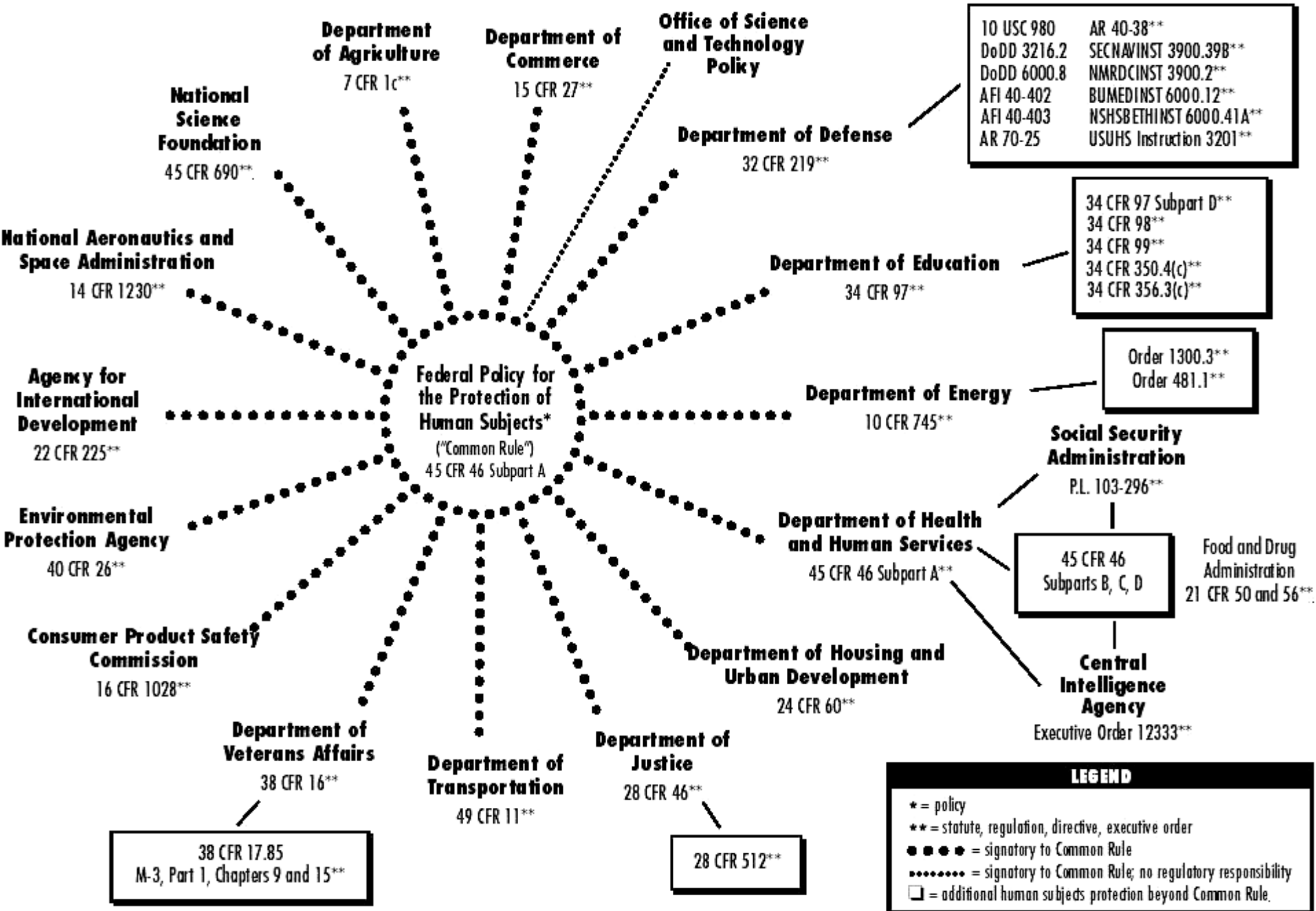


Figure C-1: Common Rule and Agency-Specific Human Research Protection Regulations



Harmonization Efforts

- Harmonization difficulties:
  - Incomplete coverage within the U.S. regulations
    - Leads to lack of guidance for U.S. institutions
  - Non-overlapping issues in international documents
    - Placebos
    - Consent
    - Ethics review
    - Gender issues
    - Privacy
  - Specific issues not covered in all documents
    - Genetics
    - Health services/outcomes research
    - Social and behavioral research

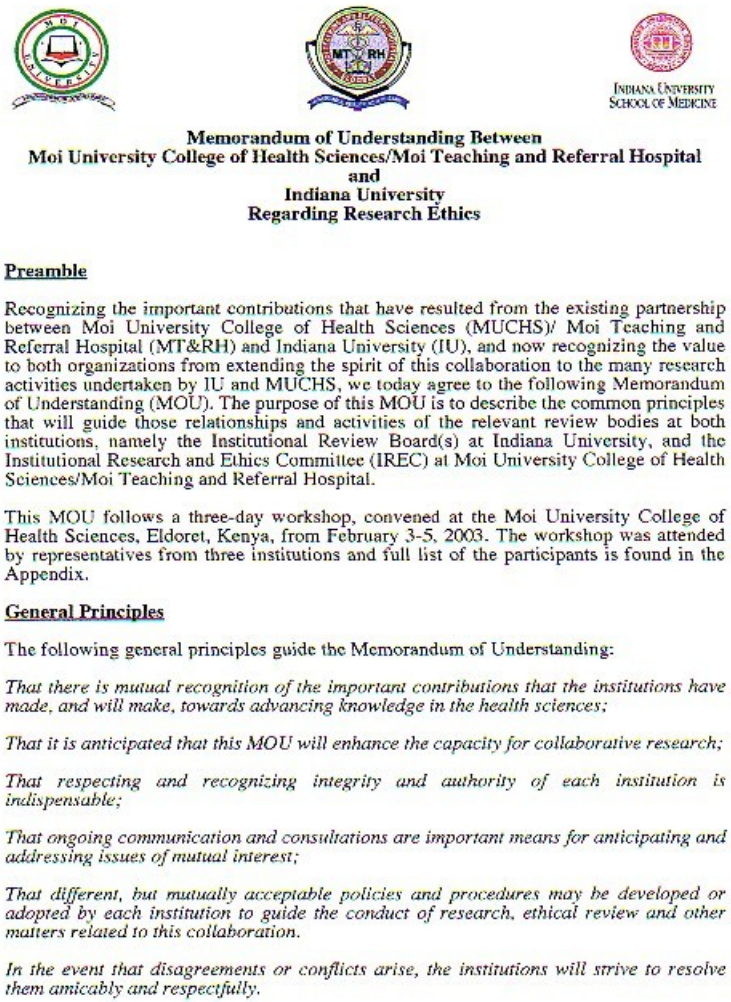
Regulatory Reform

- Equivalent protection:
  - US research regulations permit DHHS Secretary to declare that another country may substitute their guidelines for US guidelines, if the host country/institution has a system of substantive protections that are equivalent to the U.S. system
    - Is this paternalistic?
    - What of countries that have superior standards to the US?
  - However: no countries/guidelines have been determined by the U.S. to provide protections equivalent to those of U.S.

Bottom Up:
Prior Agreements

- Specifies terms and conditions of research relationship
  - Responsibilities of partners
  - Criteria for entry into a country
  - Access to post-trial benefits
  - Resolving disagreements in advance
  - Negotiations between host and sponsor
  - Enhances partnership

Bottom Up: Capacity Building



Memorandum of Understanding Between
Moi University College of Health Sciences/Moi Teaching and Referral Hospital
and
Indiana University
Regarding Research Ethics

Preamble

Recognizing the important contributions that have resulted from the existing partnership between Moi University College of Health Sciences (MUCHS)/ Moi Teaching and Referral Hospital (MT&RH) and Indiana University (IU), and now recognizing the value to both organizations from extending the spirit of this collaboration to the many research activities undertaken by IU and MUCHS, we today agree to the following Memorandum of Understanding (MOU). The purpose of this MOU is to describe the common principles that will guide those relationships and activities of the relevant review bodies at both institutions, namely the Institutional Review Board(s) at Indiana University, and the Institutional Research and Ethics Committee (IREC) at Moi University College of Health Sciences/Moi Teaching and Referral Hospital.

This MOU follows a three-day workshop, convened at the Moi University College of Health Sciences, Eldoret, Kenya, from February 3-5, 2003. The workshop was attended by representatives from three institutions and full list of the participants is found in the Appendix.

General Principles

The following general principles guide the Memorandum of Understanding:

That there is mutual recognition of the important contributions that the institutions have made, and will make, towards advancing knowledge in the health sciences;

That it is anticipated that this MOU will enhance the capacity for collaborative research;

That respecting and recognizing integrity and authority of each institution is indispensable;

That ongoing communication and consultations are important means for anticipating and addressing issues of mutual interest;

That different, but mutually acceptable policies and procedures may be developed or adopted by each institution to guide the conduct of research, ethical review and other matters related to this collaboration.

In the event that disagreements or conflicts arise, the institutions will strive to resolve them amicably and respectfully.

- MOU between Moi University College of Health Sciences and IU School of Medicine
- Followed a 3-day workshop in Kenya in 1993
- Extensive discussions about research protocols and common problems

What Makes International Research Ethical (Or Unethical)?

- An Initial list
  - Compliance with substantive and procedural protections
  - Attention to the difficulties in accommodating cultural issues
  - Appreciation of the dialectic that occurs in all international relations
  - Recognition of the risk of imposing a “double standards”
  - The challenge of pragmatic vs. aspirational arguments