Justification of Research in Humans

• Impossible to reach the important conclusions without studying humans
  • Human physiologic studies, because animal responses often are not the same
  • Epidemiological studies, because they depend on human susceptibilities and human interactions
  • Agents for treating humans because animal experiments don’t always predict results
Justification (2)

- If you’re going to treat humans, you must study humans

- Corollary: If you’re going to treat certain kinds of humans, then you must perform studies with them, for example

- Children, mentally impaired, ethnic groups, elderly, women, and pregnant women
CONFLICTING PUBLIC HEALTH GOALS

- Protect the uninfected
- Protect the infected
ETHICS

The ethics of taking action vs. the ethics of avoiding action
Definition of Ethics

• Ethics:
  • The discipline of dealing with what is good and bad, with moral duty and obligation
  • A set of moral principles or values
  • The principle of conduct governing an individual or group

• Webster’s Ninth New Collegiate Dictionary
History of the Ethical Research Movement
The Nuremberg Code (World War II)

- **Informed consent** is absolutely essential
- Qualified researchers must use appropriate research designs
- There must be a favorable risk/benefit ratio
- Participants must be free to stop at any time
The Declaration of Helsinki
World Medical Association

- "The well-being of the subject should take precedence over the interests of science and society"
- Consent should be in writing
- Use caution if participant is in dependent relationship with researcher
- Limited use of placebo, especially if treatment is available
- Greater access to benefit once research is concluded

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

• Respect for persons
• Beneficence
• Justice

Nuremberg => Helsinki => CIOMS

- Informed consent
- Research in developing countries
- Protection of vulnerable populations
- Distribution of the burdens and benefits
- Role and responsibilities of ethics committees
Basic Concepts for Ethical Research
Basic Principles of Research on Human Subjects
(The Belmont Report)

- Respect for persons
- Beneficence
- Justice
Basic Principles of Research on Human Subjects (1)

- Respect for persons
  - Choices of autonomous individuals should be respected
  - People incapable of making their own choices should be protected
  - Voluntary subjects need adequate information for decision-making
Basic Principles of Research on Human Subjects (2)

- **Beneficence**
  - Participation in research is associated with a favorable balance of potential benefits and harms
  - Maximize possible benefits, minimize potential harm
Basic Principles of Research on Human Subjects (3)

• **Justice**
  
  • Participation in research is associated with a favorable balance of potential benefits and harms
  
  • May not exploit or exclude vulnerable individuals who may benefit without good reason
Summary - Principles and Foundations of Research Ethics

- All codes and regulations advocate 3 fundamental principles:
  - Respect for persons
  - Beneficence
  - Justice
- Research is a privilege, not a right
- The well-being of the participant is paramount
Assessment of Benefits and Risks
Assure That Benefits Outweigh Risks

- Research must be justified on the basis of a favorable benefit/risk assessment for the research participant. Benefits must outweigh risks.

- This is similar to the principle of beneficence or “do no harm.” Researchers must protect participants from harm and maximize their well-being.
Risk and Benefit Defined

• A “risk” refers to a harm or likelihood of a harm. The degree of severity of a possible harm may be unclear.

• A “benefit” refers to a positive value that accrues to the participant and/or to the society. The precise degree of gain that might accrue to the participant and/or to the society may be uncertain.
Types of Risks and Benefits

- Risks or harms and benefits may be physical (pain or injury), psychological, social, economic, or legal.
- Risks or benefits of research may apply to individual participants, families, groups or organizations, communities, or nations.
- Risks and benefits to the research participant usually carry the most weight.
General Principles

• There is absolutely no justification for inhumane treatment of participants.

• Risks to participants should always be reduced to the maximum extent possible.

• If a significant risk is involved, justification of the research must be examined with particular care.

• Whenever vulnerable persons are participants, the need to involve them must be carefully demonstrated.
ETHICAL PROCEDURES FOR INTERNATIONAL RESEARCH (U.S. PUBLIC HEALTH SERVICE)
**FWAs**

Institutions that want to engage in research that do not have an IRB/IEC may submit a Federalwide Assurance form that designates one or more approved IRBs that are already registered with OHRP.
IRB Authorization

Reliance on another institution's IRB/IEC must be documented by a written agreement that is available for review by OHRP upon request. OHRP's sample IRB Authorization Agreement may be used for this purpose, or the institutions involved may develop their own agreement. Future designation of other IRB(s)/IEC(s) requires update of the FWA.
Foreign IRB Approval

Following approval of the FWA by OHRP, the research project must be reviewed by the designated IRB/IEC and an approval letter issued listing the IRB number and the FWA number of the institution conducting the research, and signed by the IRB/IEC chair.
Multiple FWAs

Funded projects may be required to get multiple FWAs if they "engage" other institutions or their employees as partners or participants in the project (see OHRP website for definition of "engagement"). Permitted use of other institutions' facilities does not constitute engagement.
Ethics Course Requirement

All investigators (including non-U.S. investigators) must complete an approved ethics training course and obtain a certificate of completion (approved courses and completion certificates are available on the web) before their proposals can be approved by the IRB/IEC.
RESEARCH IN POPULATIONS AND COMMUNITIES WITH LIMITED RESOURCES
TWO RESPONSIBILITIES

• Prior to conducting research in a population or community with limited resources the researcher/sponsor should:

  1) Ensure the research responds to the health needs and priorities of the target community.

  2) Ensure any product developed will be made available to the community.
RESPONSIVENESS TO COMMUNITY HEALTH NEEDS

- It is not sufficient to determine disease prevalence and that new research is needed.
- If successful interventions result from the research they must be made available to the community.
- If this is not done, the research is exploitative.
MAKING A PRIOR OR AGREEMENT

• Before the research begins, a plan should be offered in which the proposed product is made available to the host nation upon completion of the study.

• Participants should include representatives of the nation’s government, local authorities, community members, and NGO groups.
The agreement should include payments, royalties, distribution costs, subsidies, technology, and intellectual property.

In some cases, international organizations, public and private, may also be included in the discussions.
THE ETHICS OF CONDUCTING RESEARCH IN DEVELOPING COUNTRIES

- When, if ever, should investigators use the standards of care/ethics of developing countries vs. developed countries (e.g., Tanzania drug trials)?
- Are investigators responsible for the health of their participants?
- Can participants in developing countries understand informed consent (e.g., is there an expectancy of benefit or treatment even if not stated in the informed consent)?
- Is it ethical to do research in developing countries on issues relevant to developed countries but not relevant to developing countries?
REQUIREMENTS FOR COMMUNITY APPROVAL

• Community must have legitimate, empowered spokesperson(s)
• Community must have a common health-related culture
• A communication network for the community must be in place
FACTORS INFLUENCING VOLUNTARY CONSENT

- Vulnerability to incentives
- Impact of community pressure
- Power of investigators to influence
- Ability of participants to understand goals and risks
RESEARCH CONTROVERSIES IN DEVELOPING COUNTRIES

• Are placebo groups ethical?
• Should placebos reflect international or local standards of care?
• Should participants be assured care beyond the trials – if so, for how long?
• Should care be provided to the trial community?
• Should trials be evaluated for scale-up feasibility before implementation?