



Research Ethics

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Family , Women and Children's Health Cluster



UNDP · UNFPA · UNICEF · WHO · World Bank
Special Programme of Research, Development
and Research Training in Human Reproduction

Outline



1. A full ethics workshop
2. Ethics – the basics
3. Ethics – thoughts on guidance
4. Addressing multiculturalism

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Research ethics workshop topics

❖ Core components:

- ❖ The need for ethical review - “research” defined
- ❖ Informed consent and the informed decision-making process
- ❖ Risk and benefit assessment
- ❖ Standard of care debate

❖ Special issues:

- ❖ Concepts of vulnerability
- ❖ Cultural & ethical relativism
- ❖ Multi-national research and post-trial/ “fair benefits” debates
- ❖ Unique situations in social science research

❖ Ethics review committees/ Institutional review boards:

- ❖ Roles & responsibilities
- ❖ Implementation/ Process of scientific & ethics review of research
- ❖ Challenges



The fields of Ethics - More often reactionary, than proactive

“It took the cruelty described at Nuremberg to make the world realize it had to do something that would protect human subjects from inhumane research.”

John Bryant (Past President, CIOMS, 2000)



Ethics workshop format: Collaborative & Interactive

- ❖ **Plenary presentations**
- ❖ **"Break-out" interactive sessions to review scenarios**
- ❖ **Discussions and role-playing**
 - ❖ participants, community members, researchers, ethics committee members, monitors, member of ministries/academic institutions, & industry
- ❖ **A full mock-IRB session**

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Do we really need to do research
on humans?

Do *you* really *need* to do the
research you have designed?
- or -
how you have designed it?



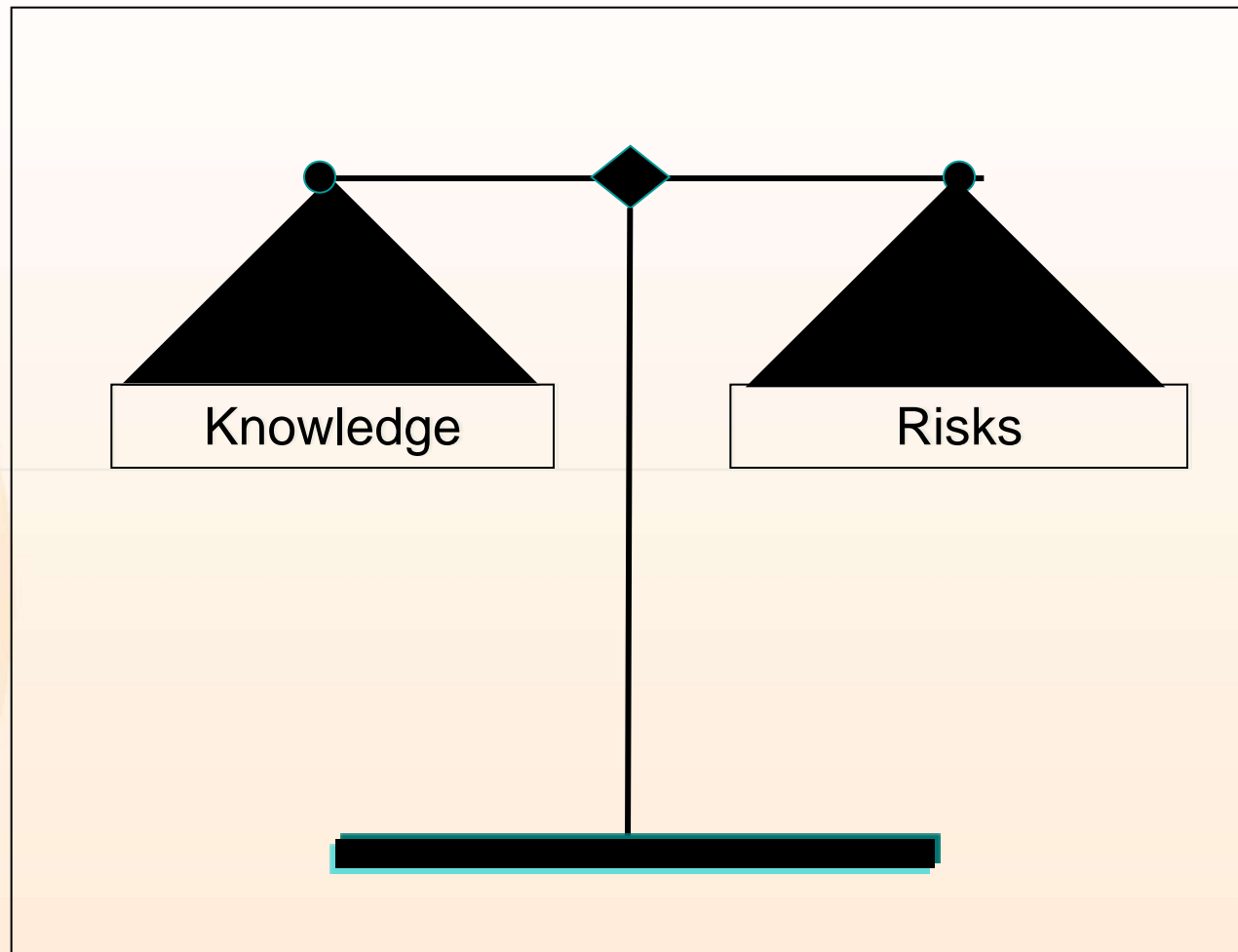
WHO Definitions for “Research”

- ❑ *Research* is defined by the WHO-ERC as:
 - ❑ any social science, biomedical, behavioural, or epidemiological activity that entails systematic collection or analysis of data, with the intent to develop or contribute to generalizable knowledge. Generalizable knowledge consists of theories, principles or relationships, or the accumulation of information on which they are based, that can be corroborated by accepted scientific methods of observation and inference.

- ❑ *Research* is defined by the WHO Strategy on Research for Health as:
 - ❑ the development of knowledge with the aim of understanding health challenges and mounting an improved response to them. This definition, in the research for health strategy, covers a spectrum of research, which spans five generic areas of activity: measuring the problem; understanding its cause(s); elaborating solutions; translating the solutions or evidence into policy, practice and products; and evaluating the effectiveness of solutions

Ethical Dilemma ...

For
researchers
and
participants.



Research ethics is not (only) the informed consent form

Informed Consent & the Decision-making Process

There is a distinction between:

informed consent (documentation), & the
informed decision-making process

Informed decision-making process includes:

all aspects leading to informed consent, & to
informed dissent



Informed decision-making requires some complexity:

The decision *by the participant* to be:

- based on competence (ability to understand)
- voluntary (free of coercion, undue influence, intimidation or inducement)
- aware and acknowledge risk and benefit of participation

Information *from the investigator* to be:

- comprehensive (complete)
- comprehensible (simple language)

Complexity in the Guidance of Research Conduct:

Deconstructing that complexity with use of the Belmont Principles

Respect for persons

Consent

Access to information

Privacy

Autonomy

Protection of confidential information

Beneficence

Harms/Risks & Benefits

Justice

Fairness, Rights

Respect for persons

Implications in SRH research

- ❑ Information revealed may be extremely disturbing for the participant (e.g. fears, violence, incest, rape)
- ❑ Research may include those who have unique vulnerabilities (e.g. children/ adolescents, trafficked persons, disabled, persons under pressure/stress)
- ❑ Information about sexual matters can be deeply personal and private
- ❑ Information **received** may be deeply distressing for the **research worker**

Respect for the person:

Maintaining Confidentiality: Legal implications

- ❑ Sensitive information may be obtained: about collateral illegal activities, drug use
- ❑ Will the information gathered harm or place at risk the participants or/and the researchers?
- ❑ Statutory duty to inform the authorities
- ❑ Court order to compel disclosure



Respect for persons: Commercial Sex Workers & the Researchers

- ❑ Maintaining confidentiality
- ❑ Maintaining respect
 - Participants viewed the researcher as “*naïve, straight-laced, judgmental and fundamentally different.*”
 - The researcher questioned her own role as “*voyeuristic, exploitive, emotional, and vulnerable.*”

Miller J. Researching violence against street prostitutes. Methodological and personal perspectives.

Beneficence: Harm and Benefits

- ❑ Does the research help the participants?
- ❑ Can the research be used against the participants?
- ❑ How is the research beneficial?
 - Can the identified gaps in knowledge be addressed by the research?

Paragraph 5, Helsinki Declaration (2008): “...well being of the participants should take precedence over the interests of science and society.”

Beneficence: not just to participants but to groups (communities, schools, workplace, hospitals...)



Harm from Stigmatization

Researchers must evaluate whether or not their research could result in such group harms and, if a possibility must minimize this risk.

Researchers must be cognizant of risks of double stigmatizations:

- Association of a husband with intimate partner violence if wife is interviewed on the subject
- Association of risky behaviour of teens to a particular school or community
- Association of HIV/AIDS with homosexuality
- Association of HIV/AIDS and/or STIs with sex workers
- Association of HIV/AIDS and/or STIs with the infertile

Justice

- ❑ People should be treated fairly.
- ❑ Selection of research participants, must be unbiased and fair.
- ❑ Examples of injustices:
 - Potentially risky research for undesirable vulnerable groups
 - Potentially beneficial research for favoured groups

**The prospect of gaining new scientific knowledge
need not
&
should not
be pursued at the expense of human rights.**

Outline

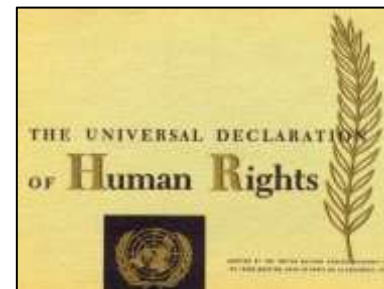


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Research Ethics is not (only) Research Ethics Committee Review

Ethics: based on Human Rights

Equality, Health, Privacy, Non-Discrimination including the Areas of Economic, Social and Cultural Rights



- ❑ Universal Declaration of Human Rights, adopted Dec. 10, 1948, G.A. Res. 217A (III), U.N. Doc. A/810, Art. 2 (1948).
- ❑ International Covenant on Civil and Political Rights, *adopted* Dec. 16, 1966, G.A. Res. 2200A (XXI), UN GAOR, 21st Sess., Supp. No. 16, U.N. Doc. A/6316 (1966), 999 U.N.T.S. 171, Art. 6(1) (*entered into force* Mar. 23, 1976) [ICCPR];
- ❑ International Covenant on Economic, Social and Cultural Rights, *adopted* Dec. 16, 1966, G.A. Res. 2200A (XXI), UN GAOR, 21st Sess., Supp. No. 16, U.N. Doc. A/6316 (1966), 993 U.N.T.S. 3, Art. 12 (*entered into force* Jan. 3, 1976) [ICESCR];
- ❑ Convention on the Elimination of All Forms of Discrimination against Women, *adopted* Dec. 18, 1979, G.A. Res. 34/180, UNGAOR, 34th Sess., Supp. No. 46, U.N. Doc. A/34/46, 1249 U.N.T.S. 13, Arts. 12, 14 (*entered into force* Sept. 3, 1981) [CEDAW];
- ❑ Convention on the Rights of Persons with Disabilities, *adopted* Dec.13, 2006, G.A. Res. 61/106, U.N. Doc. A/RES/61/106 (2006), 1249 U.N.T.S. 13, Arts. 10, 25 (*entered into force* May 3, 2008) [CRPD]
- ❑ Concluding Observations of the Committee on the Rights of the Child: Armenia, para. 38, U.N. Doc. CRC/C/15/Add.119 (2000); Convention on the Rights of the Child

Research Ethics Deliberations, guided by:

- ❑ International Ethical Guidelines for Biomedical Research Involving Human Subjects, Geneva, Switzerland: Council for International Organizations of Medical Sciences (CIOMS), 2002
- ❑ International Ethical Guidelines for Epidemiological Studies, Geneva, Switzerland: Council for International Organizations of Medical Sciences (CIOMS), 2009
- ❑ UNAIDS/WHO Ethical Considerations in biomedical HIV Prevention Trials – UNAIDS/WHO guidance document. Geneva, Switzerland: Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO), 2007
- ❑ UNAIDS/AVAC. Good Participatory Practice Guidelines for Biomedical HIV Prevention Trials. Geneva, Switzerland: Joint United Nations Programme on HIV/AIDS (UNAIDS) and the AIDS Vaccine Advisory Council (AVAC), 2007
- ❑ WHO Handbook for Good Clinical Research Practice (GCP), Guidance for Implementation. Geneva, Switzerland, WHO, 2005.
- ❑ WHO Ethical and Safety Recommendations for Researching, Documenting and Monitoring Sexual Violence in Emergencies. Geneva, Switzerland, WHO, 2007
- ❑ World Medical Association. Declaration of Helsinki: Ethics Principles for Medical Research Involving Human Subjects, Helsinki, Finland, 1964 (Latest revised version, 2008 – currently in a new draft revision, 2013)

Research Ethical Committee: guided by Standards/Operational Guidance

“Standards and operational guidance for ethics review of health-related research with human participants”



Ethical debates: Implementation Research

If a protocol for an intervention can be considered the “standard of care” then studying its implementation in a new setting may be considered Quality Improvement rather than Research:

- ❑ Protocol may not (or need not) be submitted to a Research Ethics Committee for review
- ❑ Need not be compared with an existing intervention in that hospital or unit or community setting
- ❑ Would not require informed consent
(for example, from patients who are being viewed through study and evaluation of medical records, from seriously ill patients or their representatives, from participants in Implementation Research studies which are evaluating providers or are scaling-up care - especially large scale comparisons across health system clusters.)

Ethical Debates: Controversial Issues in Social Science Research

- **Issue 1:** The use of '*mystery clients*' for obtaining information or knowledge due to the element of deception involved.
 - This deception violates the normal ethical rules regarding informed consent.
- **Issue 2:** The assessment of interventions that may be *illegal* within the community.
 - The subsequent risk this poses to the participant, other individuals involved or the community.
- **Issue 3:** The *release of information* by a participant *that reflects illegal behaviour or activity*
 - The *necessity to report* to local legal authorities *must be addressed prior to participant participation*.

Is there a place for covert research?

- | | |
|--|--|
| <ul style="list-style-type: none">• No, not under any circumstances | <ul style="list-style-type: none">• Yes, if the study has been reviewed and proper approval has been obtained.• Justifications for covert research studies may include:<ul style="list-style-type: none">– Research is of compelling importance– Safety concerns for participants and researchers have been addressed– Benefits for the individual participant– Avoiding social desirability bias |
|--|--|

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The debate

- ❑ The world contains a vast number of cultures with varying customs and traditions
- ❑ Multinational research is a global enterprise
 - Sponsors include industry, industrialized country agencies, international organizations

Can universal ethical principles be applied to these culturally diverse settings ?

Cultural Sensitivity

- A widely held view:
Researchers and sponsors need to be “culturally sensitive”
- *“The general duty of respect implies a duty to be sensitive to other cultures....The variety of beliefs and practices that exist may challenge the notions of overarching ethical principles.*
- *This in turn prompts an analysis of the relationship between the requirement of sensitivity to cultural differences and the concept of moral relativism”*

Nuffield Council on Bioethics, The Ethics of Research Related to Healthcare in Developing Countries (London: Nuffield Council on Bioethics)

Types of ethical relativism

1. Descriptive ethical (cultural) relativism
2. Normative ethical relativism
3. Meta-ethical relativism
4. Epistemological relativism
5. Contextual relativism
6. Risk-benefit relativism

1. Descriptive relativism

- Cultural-ethical relativism
 - Customs, traditions, moral beliefs, acceptable modes of conduct, and moral codes vary greatly throughout the world
 - Cultural norms and traditions are the prime source for the moral views of individuals
 - Each society has its own view of what is morally right and wrong, and these views vary from society to society
 - “What is *believed* to be right in one society is *believed* to be wrong in another”

2. Normative ethical relativism

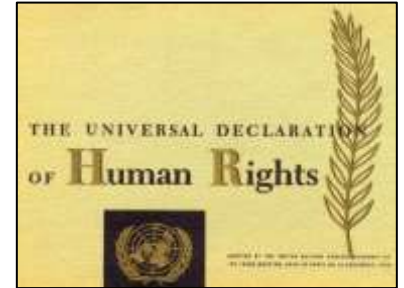
What is right in one society may be wrong in another

– Intended as a normative claim: “What *actually* is right in one society *may actually be* wrong in another*”

- ❑ Normative ethical relativism is the only position consistent with the facts of descriptive relativism
- ❑ There are no universally valid ethical principles
- ❑ It is wrong to criticize or seek to impose one culture’s *ethical norms* on another

**a moral judgment*

3. Meta-ethical relativism (1)



- Conceptual relativism
 - Moral concepts vary from culture to culture and therefore the moral judgments of one society are meaningless or unintelligible to another.
 - A culture lacking the concept of human rights cannot understand the idea of individual freedom as a basic right
 - A culture lacking the concept of gender equality cannot understand the idea of women’s rights



3. Meta-ethical relativism (2)

- Methodological relativism
 - Different cultures use different methods of reasoning to justify moral judgments
 - A culture that views ancient religious texts as the source of moral judgments may not understand the use of modern secular reasoning to justify moral judgments*

** This is not a criticism - just depicting how the basis for reasoning to reach judgments can differ*

4. Epistemological relativism

- Some cultures maintain traditional beliefs about causes and potential cures of disease
 - Ignorance or rejection of modern scientific explanations of etiology of diseases
 - Belief in spiritual cures or ritualistic healing practices
- Is it possible to obtain genuinely informed consent to participate in biomedical research in those societies?
 - If not, should research be excluded from being conducted in such settings?

5. Contextual relativism

- Need to distinguish between
 - Specific rules or norms in moral codes of different societies, and
 - Ultimate moral principles
- Actions or practices in one society may be ethically justified by the utilitarian principle
- *But* those same actions or practices may be ethically unjustifiable in another society by use of the same general principle

Clarifying concepts of ethical guidance



Confusion between :

Absolutism:

Exception-less moral rules and guidance exist that are valid for all cultures at all times and places

- Moral rules are specific but may have only very defined exceptions

Universalism:

*Fundamental moral principles exist that are universally **applicable***

- Because moral principles are general, and require interpretation

Ethical imperialism

Attempts to impose “Western” ethical principles on “non-Western” cultures constitute ethical imperialism

QUESTION:

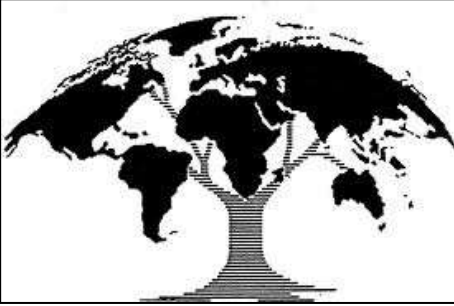
- Should researchers and sponsors attempt to impose the universal principle, “respect for autonomy” on non-Western cultures that do not recognize individual autonomy ???

Cultural relativism and research ethics

Can the principles of research ethics be universally applied?

QUESTION:

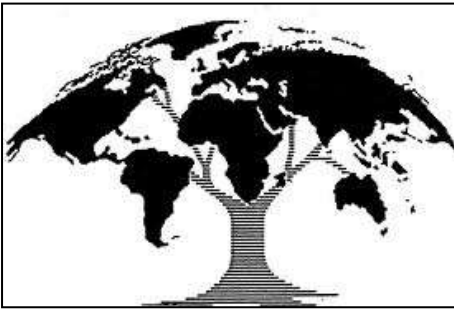
- Does the principle require that informed consent be obtained from each individual participant, even if a culture does not recognize or respect the autonomy of each individual?



Ethical imperialism & informed consent

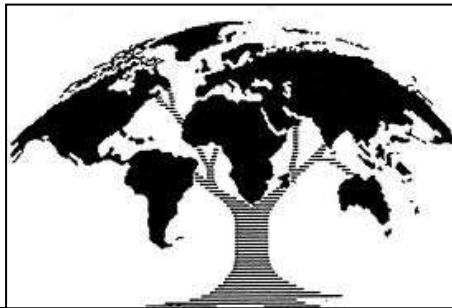
“It is ethical imperialism at its worst to assume that the informed consent requirement, which does indeed serve one (only one) moral principle in the Western setting, is in itself such a universal ethical standard.”

- Lisa H. Newton, Ethical imperialism and informed consent, *IRB: A Review of Human Subjects Research*, Vol. 12 (May-June 1990)



Ethical Debate

- ❑ **“Ethical imperialism”** could be viewed as a slogan used against those who seek to conduct or justify research to which others have ethical objections.
- ❑ Genuine ethical disagreement remains concerning the question of whether some research that may not be conducted for ethical reasons in industrialized countries may nevertheless be conducted in developing countries.



Ethical imperialism & informed consent

Two situations defended by relativists that depart from accepted ethical standard for informed consent:

- Perceived need to withhold key information from potential research participants
- Cultural custom of requiring husbands to sign consent forms for research in which their wives are participants

6. Risk-benefit relativism

- ❑ Research not ethically acceptable in one country may be ethically acceptable in another country based on different risk-benefit ratios.
- ❑ Examples:
 - Spousal/Authority consent, assent or permissions
 - Vaccine research
 - Breast cancer research
 - Placebo-based research

The Spouse: Addressing risk-benefit during moral analysis

- Some cultures maintain the custom of requiring husbands to sign consent forms for their wives to participate in research
 - Requirement exists as well for medical treatment
- Researchers in these countries typically accept the requirement
 - Sometimes, informed consent forms will have a line for a husband's signature

HRP guidance

Reproductive Health and Research/ Special Programme of HRP

Reproductive Health Research & Partners' Agreement

“A requirement of partner agreement or authorization for an individual to participate in research violates the autonomy of research subjects and their right to confidentiality.

Therefore, as a matter of ethical principle, a requirement of partner agreement or authorization should not be permitted in studies supported by [this] Programme.”

HRP Guidance – impossible to achieve ? Aspiration versus pragmatism ?

“Because of existing cultural, religious, political or legal constraints, it is sometimes impossible to achieve the ethical ideal and exceptions to this general principle may have to be accepted....”

HRP guidance does include “exception” clauses:

- ❑ *“An example would be the impossibility of recruiting any research subjects for a study in a particular country without partner agreement and the subsequent impossibility of gaining approval in that country for a new contraceptive drug or device.”*
- ❑ *“If failure to conduct the research would result in an inability of people in that country to receive the benefits of the drug or device, this consequence might be judged as sufficiently negative for the common good of the public to outweigh the usual prohibition against partner agreement for the individual participant.”*

CIOMS - International Ethical Guidelines

- ***“Only the informed consent of the woman herself is required for her participation. In no case should the permission of a spouse or partner replace the requirement of individual informed consent.***
- ***“If women wish to consult with their husbands or partners or seek voluntarily to obtain their permission before deciding to enroll in research, that is not only ethically permissible but in some contexts highly desirable. A strict requirement of authorization of spouse or partner, however, violates the substantive principle of respect for persons.”***

CIOMS, Guideline 16, Commentary

Permission from a community leader

In many societies, permission must first be obtained from a community leader, tribal chief, or council of elders before researchers may enter and approach individuals

- This process is mistakenly referred to as “community consent.” This is no different, in principle, from *permission* gained from a school principal or factory owner to enter the premises in order to conduct research
- However, this is not “*consent to enroll participants,*” it is *permission to enter the community, school or factory.*”

Community permission vs individual consent

- ❑ “Where culture or custom requires that permission of a community representative be granted before researchers may approach potential research participants, researchers should be sensitive to such local requirements.”
- ❑ *“However, in no case may permission from a community representative or council replace the requirement of a competent individual's voluntary informed consent.”*

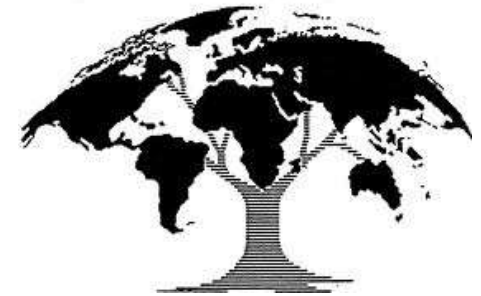
NBAC Recommendation 3.6



Vaccine Research- Addressing risk-benefit during moral analysis

- ❑ A vaccine with serious side effects has the potential for causing harm to healthy children
- ❑ The rate, of equally serious harm or even death from a disease that the vaccine is designed to prevent, may differ considerably in the two countries
- ❑ Therefore, research on the vaccine may be:
 - ethically unacceptable in the country with a low disease prevalence
 - but ethically acceptable in the country with high prevalence

Relativists' defenses



- ❑ Departures from widely accepted ethical standards are justified by the cultural context in the country or community where the research is carried out
 - Cultural relativism
- ❑ It would be impossible to conduct research without these deviations from “Western” requirements
 - Pragmatic defense
- ❑ Requiring adherence would result in a loss of contributions to medical science and lack of consequent benefits to the population in those countries or communities
 - Appeal to justice

Substantive vs. procedural requirements

Substantive ethical requirements embodied in fundamental principles of bioethics:

Respect for persons, Beneficence & Justice.

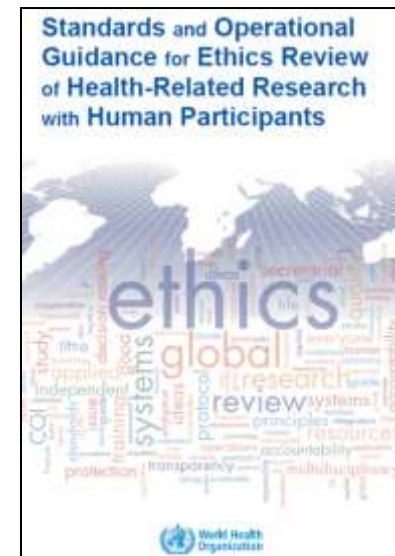
These constitute ethical *standards/principles*, and should be applied universally ...

- Requirement to obtain informed consent individually from each adult participant
- Need to disclose complete information about the research maneuvers to be performed and the expected risks of those interventions

Substantive vs. procedural requirements

Procedural ethical requirements

- May vary according to cultural and other differences
 - Requirement for **written documents** in the consent process
 - Requirement that written informed consent documents **be signed by participants**
 - **Member composition** of ethical review committees
 - **Rules of Procedure** of ethical review committees



Conclusions (1)

- Ethical principles governing research involving human participants are universally applicable
 - Yet *procedural mechanisms for implementing the principles may differ* from place to place
- Departing from ethical principles can not be justified by using custom, culture, and tradition as a reasoning.
 - Culturally sensitive approaches can show “respect for cultures” without violating fundamental ethical principles

Terminology

- ❑ MUST versus SHOULD versus MAY
- ❑ HUMAN SUBJECT versus HUMAN PARTICIPANT
- ❑ PARTICIPANT versus PATIENT (versus SUBJECT)
- ❑ RESEARCH versus THERAPEUTIC INTERVENTION

The most important thing in communication is hearing what isn't said.
Peter Drucker

Traditional belief systems can affect participant *understanding* of “research”

- ❑ When research participants are unacquainted with the concepts and methods of clinical/biomedical “research”
 - To preclude the possibility of performing research in these communities could deny members of such societies the eventual benefits of research.
 - Researchers should seek creative ways of presenting information
 - For example, using analogies readily understood by the population
- ❑ **Major danger:**
- ❑ Such individuals may be completely unaware they are participants in research. Research that may not benefit them and may even harm them.

(NOTE: The majority of RCTs do *not* show benefit in the new intervention arm.)

Conclusion (2)



- ❑ Ethics in research is more than obtaining informed consent from participants.
- ❑ Research ethics considerations and dialogue/debate must include basic ethical principles - which should be applied highly contextually.
- ❑ Outcome and decision-making on ethical issues will change/evolve - over time and as settings/populations and terminology changes.

Omissions

A few key topics not discussed/mentioned:

- ❑ Ethical conduct of researchers, their supporters and sponsors ---
From project initiation, monitoring, reporting & disseminating results of the research.
- ❑ The interplay between ERCs, DSMBs and National Regulatory Bodies/Agencies - When they do or do not agree & the researchers recourse.