



An overview to the development and philosophy of research ethics

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Literature cited

- International regulations and Guidelines
- US Regulations and Guidelines
- European regulations and guidelines
- *Roberto Rivera, David Borasky, Robert Rice, Florence Carayon, Family Health International*
- Zulfiqar Ahmed Bhutta: International declarations and guidelines on Research with Human Subjects: issues and controversies



Overview

- **Principles of Research Ethics**

- **Foundations of Research Ethics**
- Historical aspects of codes of conduct in medical practice and research
 - International Declarations & Guidelines

Learning Objectives:

**Learn about the 3
Fundamental principles of
Research ethics**

**Learn about Foundations of
Research Ethics**





Principles of Research Ethics

- ❑ The researcher sets as a primary goal the protection of research volunteers while at the same time incorporating ethical considerations for project design and implementation.
- ❑ The principles of research ethics have grown out of abuses in the past.
- ❑ Today a great amount of attention is directed at research that involves human participants.
- ❑ International research ethics ensure that research conducted at the local level follows international expectations and standards.
- ❑ Following such international expectations validates the time and energy invested by the researcher—as well as the good will and trust invested by the participants.



Fundamental Principles of Human Research Ethics

□ **Respect for persons**

□ **Beneficence**

□ **Justice**

These principles are considered universal, transcending geographic, cultural, economic, legal and Political boundaries.

Researchers, institutions, and in fact human society, are obligated to assure that these **principles are followed whenever research on humans is conducted.**



Respect for Persons

- **Autonomy, self determination**

Respect for persons recognizes the capacity and rights of all individuals to make their own choices and decisions

- **Vulnerable persons need special protection**

An important component of this principle is the need to provide special protection to vulnerable persons.

Respect for Persons (continued)

- those with limited education**
- Vulnerable groups:**
 - the poor**
 - those with difficult access to health services**
 - women**

Respect for Persons (continued)

- **Informed consent**
 - **Respect for persons is embodied in the informed consent process.**
 - Designed to empower the individual to make a voluntary informed decision regarding participation in the research.
 - Potential research participants must **fully comprehend** all elements of the informed consent process.



Beneficence

- Beneficence makes the researcher responsible for the participant's physical, mental and social well-being as related to the study.
- The risks to a person participating in a research study must be weighed against the potential benefit to the participant and the importance of the knowledge to be gained.
- In any case, all risks should be kept to a minimum.



Beneficence

- **Physical, mental and social well-being**

Beneficence makes the researcher responsible for the participants physical, mental and social well-being as related to the study.

Beneficence is also referred to as the principle of *non-maleficance*.

Beneficence

- **Risks reduced to a minimum**
- The risks to a person participating in a research study must be weighed against the potential benefit to the participant and the importance of the knowledge to be gained.
- In any case, all risks should be kept to a minimum.

Beneficence

- **Protection of the participant is overriding responsibility of the researcher**
- **Protecting the participant is more important than:**
 - • the pursuit of new knowledge
 - • the benefit to science that will result from the research
 - • personal or professional research interest

Justice

- **Distribution of risk and benefit**
- **Equitable recruitment of research participants**
- **Special protection for vulnerable groups**
- The researcher's obligation is to **distribute equally the risks and benefits of participation** in the research study.
- **Recruitment and selection of research participants should be done in an equitable manner.**
- The principle of justice forbids placing one group of people at risk solely for the benefit of another.



Foundations of Research Ethics

Guidelines, codes and regulations have been created in recent decades to guide the conduct of research involving human participants. Some of these guidelines were created in response to an ethical lapse. Others were developed to better serve the changing world of research. And still others have evolved since their creation in an attempt to provide answers to new problems and challenges created by the ever-changing research environment. Each reflects the principles of:

- **Respect for persons**
- **Beneficence and**
- **Justice.**



The Nuremberg Code

- ❑ **Informed consent is absolutely essential**
- ❑ **Qualified researchers use appropriate research designs**
- ❑ **Favourable risk/benefit ratio**
- ❑ **Participant must be free to stop at any time**
- ❑ **The code does not specifically address clinical research in patients with illnesses, an oversight addressed in later codes and regulations.**



The Declaration of Helsinki

- Source: World Medical Association
 - WMA created to restore integrity to the medical profession.
 - Focus: *physicians'* duties.
 - Declaration motivated in part by desire for professional control of research enterprise
 - Adopted 1964; amended 1979, 1983, 1989, 1996, 2000.



The Declaration of Helsinki

- Principles, not rules
- 32 short clauses, no elaboration
- Advisory only, but recognized in national legislation and WHO practices.



Helsinki: *Elements 1*

- All subjects must volunteer
- Informed consent required:
 - aims, methods, sources of funding,
 - any possible conflicts of interest
 - anticipated benefits and potential risks
 - right to withdraw consent to participate at any time without reprisal.



Helsinki: *Elements 2*

- Ethical review committee required
- Design of study to be publicly available
- No research unless “the importance of the objective outweighs the inherent risks and burdens”
- And unless “reasonable likelihood that the populations in which the research is carried out stand to benefit from the research”



Helsinki: *Incompetent Subjects*

- Research on subjects incapable of consent requires:
 - Consent of parents or guardian
 - “the research is necessary to promote the health of the population represented”
 - “this research cannot instead be performed on legally competent persons”



Helsinki: *Placebo Controls*

- “A new method should be tested against the best current ... methods”
- Placebo OK only “where no proven prophylactic, diagnostic or therapeutic method exists.”



Helsinki: *Obligations for Treatment*

- At the conclusion ... every patient should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study (par.30).

The Tuskegee trials (1932 – 1972)

- Initially supposed to last for six months!
- 13 research reports & several generations of PHS and CDC researchers
- 399 men with syphilis and 201 controls thought that they were being “treated”!
- *“As I see it, we have no further interest in these patients until they die!”* (Dr Oliver Wenger 1933)



The Belmont Report

- **Ethical Principles and Guidelines for the Protection of Human Subjects of Research:**
 - **Respect for persons**
 - **Beneficence**
 - **Justice**



Council for International Organizations Medical Science (CIOMS) Guidelines

- ❑ NGO created by WHO and UNESCO
- ❑ “Elaboration” of Declaration of Helsinki
- ❑ 15 Guidelines with extensive explanations
- ❑ Current version: 1993
- ❑ Revised version (discussed Feb 2002)



Council for International Organizations Medical Science (CIOMS) Guidelines

- **Nuremberg**
 - **Helsinki**
 - **CIOMS**
- informed consent
 - research in developing countries
 - protection of vulnerable populations
 - distribution of the burdens and benefits
 - role of ethics committees



CIOMS: Developing Countries

- No research in developing countries unless it could be carried out in developed countries
- “research is responsive to the health needs and the priorities of the [host] community”
- “any product developed will be made reasonably available to inhabitants of the underdeveloped community”



CIOMS: Clinical Trials in Developing Countries

- Phase 1 drug studies and Phase I and II vaccine studies should be conducted only in developed communities of the country of the sponsor.
- In general, Phase III vaccine trials and Phase II and III drug trials should be conducted simultaneously in the host community and the sponsoring country



CIOMS Revisions: Controversy

- Remain consistent with Declaration of Helsinki?
- Standard of Care
- What is owed after the study concludes?
- Endorse experimentation on embryos?



International Conference on Harmonisation (ICH)

- Standardize drug development and approval process**
- Protocol development standards**
- Review by ethics committee**
- Researcher responsibilities**
- Sponsor responsibilities**

National Bioethics Advisory Committee (NBAC)

(NBAC) was established by Executive Order 12975, signed by President Clinton on October 3, 1995.

NBAC's functions are defined as follows:

- NBAC shall provide advice and make recommendations to the National Science and Technology Council and to other appropriate government entities regarding the following matters:
 - 1) the appropriateness of departmental, agency, or other governmental programs, policies, assignments, missions, guidelines, and regulations as they relate to bioethical issues arising from research on human biology and behavior; and
 - 2) applications, including the clinical applications, of that research.

National Bioethics Advisory Committee (NBAC)

- b) NBAC shall identify broad principles to govern the ethical conduct of research, citing specific projects only as illustrations for such principles.
- c) NBAC shall not be responsible for the review and approval of specific projects.
- d) In addition to responding to requests for advice and recommendations from the National Science and Technology Council, NBAC also may accept suggestions of issues for consideration from both the Congress and the public. NBAC also may identify other bioethical issues for the purpose of providing advice and recommendations, subject to the approval of the National Science and Technology Council.



National Bioethics Advisory Committee (NBAC)

- Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries**
- Responsive to local needs**
- Community involvement**
- Placebo use only when justified**
- Access to benefits**
- Focus on informed consent**



The U.S. Code of Federal Regulations (also called *The Common Rule*)

- Prior approval by ethics committee
- Written informed consent and documentation
- Equitable recruitment of research participants
- Special protection for vulnerable groups
- Continuing review of approved research

- (it appears as *45 CFR 46*)

Summary: International regulation of research

International Guidelines

- Nuremberg Code
- Helsinki Declaration
- CIOMS Guidelines
- International Conference on Harmonisation
- Council of Europe
- Nuffield Council
- UNAIDS
- NBAC Recommendations
- CIOMS revisions
- Nuffield Council Report
- USA (1947)
- WMA (1964, 2000)
- WHO (1982, 1993)
- Europe (1996)
- Europe (1997)
- UK (1999)
- WHO (2000)
- USA (2001)
- Geneva (2002) draft
- April (2002)

Comparison of guidelines

	Informed Consent	Confidentiality	Obligations (Prior and Post)	Standards of Care
Helsinki	✓	✓	✓	✓
CIOMS	✓	✓	✓	✓
UNAIDS	✓		✓	
ICMR	✓	✓	✓	✓
Nuffield	✓	✓	✓	✓

From Fundamental Ethical Principles to Local Guidelines

**Respect for Persons,
Beneficence, Justice**

**National
regulations**

**Institution
operational guidelines**

**International
recommendations**



Local Regulations and Guidelines

- Many countries now have national guidelines**
- Rapid growth of research on a global scale**
- Greatest need is in developing countries**

National regulation of research

Developed country guidelines

- | | |
|---------------|-------------|
| □ France | □ 1988 |
| □ Denmark | □ 1992 |
| □ Finland | □ 1992-1999 |
| □ New Zealand | □ 1997 |
| □ Netherlands | □ 1998 |
| □ Canada | □ 1998 |
| □ Australia | □ 1999 |
| □ UK | □ 1998-1999 |

National regulation of research

Developing country guidelines

- South Africa
- Thailand
- Brazil
- Uganda
- China
- Tanzania
- India
- MRC SA, 1993
- MOPH, 1995
- 1996-1999
- NCC, 1997
- 1998
- 1999
- ICMR, 2000



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**