

Do the Codes Apply to My Research? Nuremberg, Helsinki, the Belmont Report, CIOMS, and the Common Rule

Ivor A. Pritchard, Ph.D.

Senior Advisor to the Director

Office for Human Research Protections

Ivor.Pritchard@hhs.gov

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Research Ethics Codes

- Nuremberg Code (1947)
- Declaration of Helsinki (1964/2008/Now)
- The Belmont Report (1979)
- Council for International Organizations of Medical Sciences (CIOMS)(1982/2002)
- The Common Rule (45 CFR Part 46, Subpart A, 1974/1991/Now)

MORE Research Ethics Codes

- 45 CFR Part 46 Subparts B, C, D
- 21 CFR Parts 50, 56, 312, 812 (FDA)
- HIPAA, FERPA, PPRA, CIPSEA,
- ICH E6 GCP
- Maryland State Law: House Bill 917 “Human Subject Research - Institutional Review Boards”, (and New York, California, etc....)

AND MORE Research Ethics Codes

- Hippocratic Oath (5th Century BCE)
- American Medical Association (2001)
- American Nursing Association (2001)
- American Psychological Association (2010)
- American Education Research Association (2011)
- See: OHRP International Compilation at <http://www.hhs.gov/ohrp/international/intlcompilation/intlcompilation.html>

Nuremberg Code

- “The voluntary consent of the human subject is absolutely essential.”
- Investigator responsibility
- Fruitful results
- Avoid suffering and injury
- Subject or Investigator may discontinue

Declaration of Helsinki (2008)

- “...the well-being of the individual research subject must take precedence over all other interests.”
- Some subjects are incapable of consent.
- Placebo trials are ethical *sometimes*.
- Prospective committee approval is required.
- Under-represented populations should have access to participation.
- Vulnerable populations who participate should also benefit.

CIOMS

Applies the Declaration of Helsinki to research in under-developed/low resource countries.

- Scientific and ethical review are inseparable.
- Investigators must insure subject's understanding.
- Risks to groups should be considered.

CIOMS (cont.)

- Other vulnerable groups: “...medical and nursing students, subordinate hospital and laboratory personnel, employees of pharmaceutical companies, and members of the armed forces or police...”
- “In research involving women of reproductive age...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.”

CIOMS (cont.2)

- Developed interventions should be made available to community where research occurs.
- Beneficial drugs should be provided to subjects post-study.
- Subjects injured in research are entitled to treatment and financial compensation.
- Research infrastructure capacity in developing countries should be strengthened.

The Belmont Report

- Advancement of the socially valued practice of research
- Boundary between research and practice
- Respect for Persons/Informed Consent (& Protection of Limited Autonomy)
- Beneficence/Assessment of Risks and Benefits
- Justice/Selection of Subjects

The Common Rule

The Federal Policy for the Protection of Human Subjects: Office of Science and Technology Policy; Department of Agriculture; Department of Energy; National Aeronautics and Space Administration; Department of Commerce; Consumer Product Safety Commission; International Development Cooperation Agency; Department of Housing and Urban Development; Department of Justice; Department of Defense; Department of Education; Department of Veterans Affairs; Environmental Protection Agency; Department of Health and Human Services; National Science Foundation; Department of Transportation. (Plus the Central Intelligence Agency and the Department of Homeland Security.)

Informed Consent in the Common Rule

- Informed Consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 46.116. (.111(a)(4))
- .116 requires:
 - Sufficient opportunity to consider participation
 - Minimization of coercion or undue influence
 - Information in understandable language
- .116 allows waiver of informed consent in some circumstances

Beneficence in the Common Rule

- Risks to subjects are minimized: (1) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk,...(111(a)(1))
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result....(111.(a)(2))

Justice in the Common Rule

- 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 particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.
(111(a)(3))

Minutes in the Common Rule

“(a) An institution, or when appropriate an IRB, shall prepare and maintain adequate documentation of IRB activities, including the following:

.... (2) Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution...” (115(a)(2))

“Human Subjects Research
Protections: Enhancing
Protections for Research Subjects
and Reducing Burden, Delay and
Ambiguity for Investigators”

(Advance Notice of Proposed
Rulemaking (ANPRM), Federal
Register, July 26, 2011)

ANPRM Proposals

- Scope of regulatory jurisdiction
- Revised tiers of review
- Single IRB review for domestic multi-site studies
- Informed Consent improvements
- Single set of security/confidentiality standards
- Biospecimen research
- Data Reporting
- Uniformity of regulatory guidance

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What does “Do the Codes Apply...” mean?



The Challenge of Applying Codes

- “The codes consist of rules, some general, others specific, that guide the investigators or the reviewers of research in their work. Such rules often are inadequate to cover complex situations; at times they come into conflict, and they are frequently difficult to interpret or apply. Broader ethical principles will provide a basis on which specific rules may be formulated, criticized and interpreted.” (Belmont)

Do the Codes Conflict?

- A recent review of 6,000 consolidated standards found general consensus, with 14 areas of potential/actual conflicts in areas such as trial design (eg. placebo control groups), inclusion of vulnerable subjects, compensation for injury, sponsor role, etc. (Kolman et. al. 2012, Journal of Law, Medicine and Ethics).

The Challenge of Applying Principles

“Three principles, or general prescriptive judgments, that are relevant to research involving human subjects are identified in this statement.... Other principles may also be relevant. These principles cannot always be applied so as to resolve beyond dispute particular ethical problems. The objective is to provide an analytical framework that will guide the resolution of ethical problems arising from research involving human subjects.” (Belmont)

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the Belmont Report, CIOMS, and
the Common Rule”

Why Does It Matter If a
Code Applies?

Federal Employee Code of Conduct

- (a) Public service is a public trust, requiring employees to place loyalty to the Constitution, the laws, and ethical principles above private gain.
- (b) Employees shall not hold financial interests that conflict with the conscientious performance of duty.
- (c) Employees shall not engage in financial transactions using nonpublic Government information or allow the improper use of such information to further any private interest.
- (d) An employee shall not, except pursuant to such reasonable exceptions as are provided by regulation, solicit or accept any gift or other item of monetary value from any person or entity seeking official action from, doing business with, or conducting activities regulated by the employee's agency, or whose interests may be substantially affected by the performance or nonperformance of the employee's duties.
- (e) Employees shall put forth honest effort in the performance of their duties.
- (f) Employees shall make no unauthorized commitments or promises of any kind purporting to bind the Government.
- (g) Employees shall not use public office for private gain.
- (h) Employees shall act impartially and not give preferential treatment to any private organization or individual.
- (i) Employees shall protect and conserve Federal property and shall not use it for other than authorized activities.
- (j) Employees shall not engage in outside employment or activities, including seeking or negotiating for employment, that conflict with official Government duties and responsibilities.
- (k) Employees shall disclose waste, fraud, abuse, and corruption to appropriate authorities.
- (l) Employees shall satisfy in good faith their obligations as citizens, including all just financial obligations, especially those such as Federal, State, or local taxes-that are imposed by law.
- (m) Employees shall adhere to all laws and regulations that provide equal opportunity for all Americans regardless of race, color, religion, sex, national origin, age, or handicap.
- (n) Employees shall endeavor to avoid any actions creating the appearance that they are violating the law or the ethical standards promulgated pursuant to this order.

Kohlberg's 6 Stages of Moral Development

1. Obedience and punishment orientation
2. Self-interest orientation
3. Interpersonal accord and conformity
4. Authority and social-order maintaining orientation
5. Social contract orientation
6. Universal ethical principles

Should I Care If the Codes Apply to My Research?

