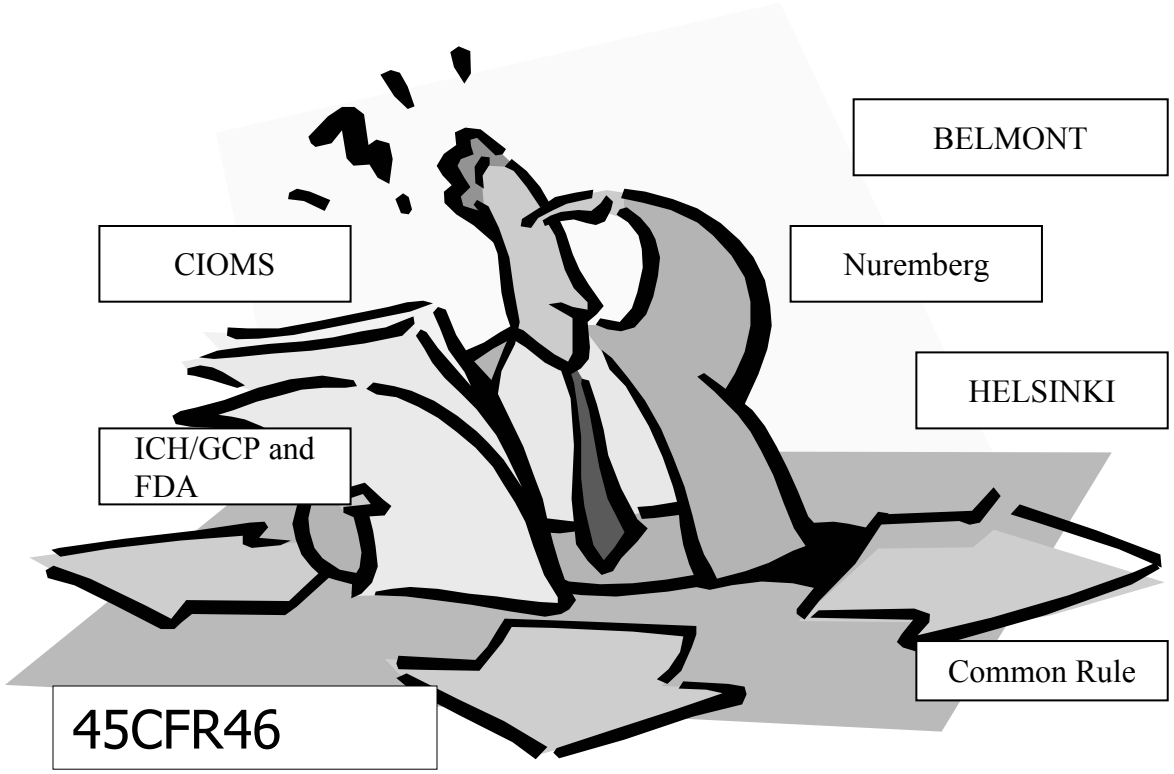
DO THE CODES APPLY TO MY RESEARCH?



Codes/guidelines: Research Ethics

- The Nuremberg Code
- The Declaration Of Helsinki
- The Belmont Report
- CIOMS/WHO International Ethical Guidelines For Biomedical Research Involving Human Subjects
- ICH/GCP-International Conference on Harmonization- Good Clinical Practice

U.S. Regulations and Guidelines

- Title 45 US CFR.46
  - The Common Rule
  - Additional subparts
- NIH Policy and Guidelines on women, ethnic minorities and children
- 21 CFR. 50 AND 56- FDA Regulations
- NIH MPA and FWA

Codes and guidelines

- Most developed in response to crisis or exposure of research abuse
- Primary focus is on protection of subjects
- Overlap
- Differences in interpretation

How are guidelines to be used?

- Fundamental principles or rules?
- Universal?
- Absolute or subject to revision and interpretation?
- "Research ethics are broader and deeper than any actual or possible regulations could encompass"

Nuremberg Code 1947

- Nazi doctor's trial
- In response to 'experiments' done with prisoners in concentration camps
- Authors were American
- 10 principles

Nuremberg Code 1947

- 1. The voluntary consent of the human subject is absolutely essential
- 2. The experiment should be such as to yield fruitful results for the good of society unprocurable by other means… and not random and unnecessary in nature

Declaration Of Helsinki

1964, 1975, 1983, 1989, 1996, 2000

- "World Medical Association has prepared the following recommendations as a guide to every physician in biomedical research*...standards as drafted are only a guide to physicians all over the world."* (1983, 1989, 1996)
- WMA has developed the Declaration... as a *statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects*" (2000)

Declaration Of Helsinki
pre-2000 contributions

- Therapeutic versus non-therapeutic research
- Independent review of the 'Design and performance of each experimental procedure-clearly formulated in a specific protocol"

Declaration Of Helsinki
pre-2000 contributions

- Explicitly allowed informed consent from a legal guardian
- Research not in accordance with Helsinki principles should not be accepted for publication.

Declaration of Helsinki (pre 2000)

- In any medical study, every patient--including those of the control group, if any--should be assured of the best proven diagnostic and therapeutic method. This does not exclude the use of inert placebo in studies where no proven diagnostic or therapeutic method exists.

Declaration of Helsinki (2000)

- The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic, and therapeutic method exists (#29)

Declaration Of Helsinki

2000 additions

- Medical research is only justified if there is a reasonable likelihood that the populations in which research is carried out stand to benefit from the research (#19).
- At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic, and therapeutic methods identified by the study (#30)

The Belmont Report

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1979

- A. Boundaries between research and practice
- B. Ethical principles underlying the conduct of research:
  - Respect for persons
  - Beneficence
  - Justice

Respect For Persons

- Individuals should be treated as autonomous agents (capable of self-determination)
- Persons with diminished autonomy deserve protection
- **Application:** Informed consent

Beneficence

- Two general complementary rules:
  - Do not harm
  - Maximize possible benefits and minimize possible harms
- **Application**: Risk/Benefit assessment

Justice

- Fairness in the distribution of the benefits and burdens of research (distributive justice)
- **Application:**
  - Fair procedures and outcomes in the selection of subjects
  - Protection of vulnerable subjects

International Ethical Guidelines for Biomedical Research Involving Human Subjects

- Council for International Organizations of Medical Sciences (CIOMS)/WHO
- Proposed guidelines 1982
- Ethical review of epidemiological studies 1991
- International guidelines 1993 and 2002
- Application of the Declaration of Helsinki in developing countries
- Externally sponsored research

International Ethical Guidelines for Biomedical Research Involving Human Subjects (2002)

- 21 Guidelines with extensive commentary
- New additions:
  - Ethical justification and scientific validity (#1)
  - Benefits and Risks (#8)
  - Limitations on risk for those who cannot consent (#9)
  - Choice of controls (#11)
  - Strengthening capacity (#20)
  - Obligation of external sponsors for health care services (#21)

International Ethical Guidelines for Biomedical Research Involving Human Subjects

- Responsiveness to the health needs and priorities of the community
- 'Reasonable availability'
- Rights of subjects to compensation for research injury

ICH Harmonised Tripartite Guideline-GCP (1996)

- Objective: "…to provide a unified standard for the European Union, Japan, and the U.S….for mutual acceptance of clinical data by regulatory authorities in those jurisdictions"
- GCP-"…an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects"

ICH-Guideline for Good Clinical Practice

- "Compliance with this standard provides public assurance that the rights, safety, and well-being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical data are credible"
- Adopted by US FDA as Good Clinical Practice: Consolidated Guideline (1997)

45CFR.46 Protection of Human Subjects

- PHS policy 1966
- National Research Act (1974)
- DHEW regulations (1981)
- The Common rule- 17 Federal agencies, including DHHS (1991)

45CFR.46 Protection of Human Subjects

- Composition and function of a local institutional review board (IRB)
- IRB to assure that risks are minimized, research risks are reasonable in relation to expected benefits, subject selection is equitable, and informed consent will be obtained from each subject.

45CFR 46.111 (2)

- "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."

45CFR 46

- Subpart B- Fetuses, pregnant women, and human *in vitro* fertilization
- Subpart C- Prisoners as subjects
- Subpart D- Children
- ?future subparts?

NIH guidelines on the inclusion of women and minorities

- NIH Reauthorization Act (1993).
- Women and members of ethnic minority groups are to be included (some exceptions)
- Outreach programs for recruitment
- Sufficient to provide for a valid analysis of differences between groups

NIH Policy and Guidelines on the Inclusion of Children as Participants in Research

"…children must be included in all human subjects research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them…" (Effective October 1, 1998)

Assurance of Compliance with Federal Regulations

- OHRP
- Assurance (MPA, now FWA)
- Guided by the Belmont Principles

FDA REGULATIONS

- Primarily found in 21CFR.56 and 21CFR.50
- 21CFR.50 Protection of Human Subjects (informed consent)
  - Subpart D on research with children
- 21CFR.56 IRB composition and function
- Minor differences from the common rule.

FDA REGULATIONS

- Part 54-Financial disclosure
- Part 312- IND applications
- Part 314- applications to market a new drug
- ICH-GCP- “represents the agency’s current thinking on good clinical practices”

Institute of Medicine

- Responsible Research: A Systems Approach to Protecting Research Participants (2002)

So, which rules must I follow?

- 45 CFR.46 –for federally funded research
- +Subparts B, C, D and NIH guidelines if funded by NIH
- +21 CFR. 50 and 56 and ICH/GCP-if testing a new drug, biologic, or device for which ultimately will seek FDA approval
- +Helsinki- if want to publish in a major medical journal

ALPHABET SOUP

- CIOMS
- MPA
- OHRP
- 45CFR46
- ICH
- OHSR
- IRB

Links to more information

- http://www.wma.net
- http://www.cioms.ch
- http://ohrp.osophs.dhhs.gov/
- http://206.102.88.10/ohsrsite/
- http://www.fda.gov/oc/gcp