CSDE 502
Human Subjects & the IRB

April 15, 2022

Institutional Review Boards: The Timeline

1947 - The Nuremberg Trials conclude & the AMA has been working on a set of research ethics for experiments with human subjects

The Nuremberg Code

- Informed consent of human subjects
- Minimization of harms & risks
- Scientific validity
- Social value

Institutional Review Boards: The Timeline

1953 - NIH opens Clinical Center in bethesda, MD & reviewed protocols to avoid harms to subjects

1965-66 - National Advisory Health Council and NIH-funded research begin required prior peer-review for human subjects research

1971 - FDA follows suit for new drugs and medical devices

Institutional Review Boards: The Timeline

1972 - Investigative journalism exposes Tuskegee study

1974 - National Research Act → Code of Federal Regulations at Title 45, Part 46 requires institutions to establish **institutional review boards** (IRBs)

45 CFR 46: Institutional Review Board

- Scientific & non-scientific
- Male & female
- Institutional & local community

Institutional Review Boards: The Timeline

1981-86 - Changing the IRB requirements

The Belmont Report

- Respect for persons
- Beneficence
- Justice

1991 - DHHS issues final federal policy

The Common Rule, 45 CFR 46

1. Minimize risks
2. Risks reasonable in relation to benefits to subjects or society
3. Seek & document informed consent
4. Select subjects equitably
5. Protect privacy & confidentiality
6. Protect vulnerable subjects
7. Provisions for data and safety monitoring

Institutional Review Boards: The Timeline

2018 - The Revised Common Rule

The Revised Common Rule

- New consent requirements
  - Whether subject's private information or biospecimens could be used for future research studies or distributed to another investigator for future research studies, with or without identifiers.
  - The subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit.
  - Whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions.
  - Whether the research will (or might) include whole genome sequencing

Institutional Review Boards: The Timeline

2018 - The Revised Common Rule

The Revised Common Rule

- Key information requirement
  - The consent process and form (if there is a consent form) must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject in understanding the reasons why one might or might not want to participate in the research. This part of the consent form or process must be organized in a way that facilitates comprehension.

Institutional Review Boards: The Timeline

2018 - The Revised Common Rule

The Revised Common Rule

- Criteria for granting a waiver of consent.
  - No more than minimal risk to subjects.
  - The research could not practicably be carried out without the waiver.
  - The waiver will not adversely affect subjects' rights and welfare.
  - The subjects will be provided with any additional pertinent information after participation.
  - **NEW** If using identifiable private information or identifiable biospecimens, could not practicably be carried out without using such information or biospecimens in an identifiable format.

Institutional Review Boards: The Timeline

2018 - The Revised Common Rule

The Revised Common Rule

- Posting of clinical trial consent form.
  - For each clinical trial conducted or supported by a federal agency that has signed the revised Common Rule, one IRB approved consent form used to enroll subjects must be posted on a publicly available federal website that is established as a repository for such consent forms. This is the responsibility of the researcher or the federal agency.

Ethical Dilemmas in Human Subjects Research

- Research vs therapy
- Risk vs benefit
- Informed consent
- Privacy and confidentiality
- Vulnerable subjects

Ethical Dilemmas: Research vs therapy

- The Belmont Report notes the importance of distinguishing research from therapy
  - If interventions are conducted in order to benefit the patient they are innovative therapy, not research
- Distinction not always obvious
  - “Undue burden on HCPs or institutions and interfere with medial or public health practice or quality improvement activities” (Shamoo & Resnik, p. 256) ??
- Data and safety monitoring board (DSMB) can stop a trial if it is too risky or so clearly effective
- Returning individualized results to research subjects
- Ancillary care & medical care following study completion

Ethical Dilemmas: Risk vs benefit

- Phase I trials usually involve health subjects to test dosing, interactions, etc.; Phase II tests efficacy, small; Phase II tests efficacy, large
- Risks must be reasonable relative to benefits of knowledge gained, no absolute limits on risk
  - Some view absolute limits on risk for adult subjects as paternalistic
  - Some argue subjects may not fully understand the risks
- No regulations on third-party or bystander risks

Ethical Dilemmas: Informed Consent

- Reasons for informed consent are clear
- What research requires informed consent?
  - The Common Rule allows IRBs to waive if research is minimal risk and subjects will be debriefed.
- Conflicts of interest not required to be disclosed
- Therapeutic misconception: potential subjects viewing research as therapy, not research → consenting to something different
- Compensation cannot be coercive, but lack of compensation can be exploitative
- Can we ever achieve true informed consent?
  - Paternalism or realism?

Ethical Dilemmas: Privacy and confidentiality

- **Privacy** is a domain of personal space, dominion, or information that one has a right to keep from the public.
- **Confidentiality** describes measures used to protect private information.
- Principles of scientific openness vs confidentiality
  - De-identified records may not be confidential, especially for subjects who are members of small groups in the population
- The Prime Directive and (mandatory) reporting

Ethical Dilemmas: Vulnerable subjects

- Individuals who have difficulty providing informed consent or protecting their own interests due to age, mental disability or illness, poverty, lack of education, language barriers, or other cultural or social factors.
  - Legally authorized representatives (LAR)
  - Assess ability to provide consent
  - Assent, if not consent
  - IRB comprised of members with expertise to evaluate research involving vulnerable populations
  - Use non-vulnerable subjects before vulnerable subjects
  - Limit risks for vulnerable subjects
- Adverse effects of being routinely excluded from research
  - Pregnant people, children, prisoners, LMICs

The UW IRB

- https://www.washington.edu/research/hsd/
- https://www.washington.edu/research/hsd/covid-19/
- https://www.washington.edu/research/hsd/do-i-need-irb-review/
- https://www.washington.edu/research/hsd/revised-common-rule/