Rules of Human Experimentation

Elaine Larson
CUMC IRB Chair
Associate Dean for Research, School of Nursing
Professor of Epidemiology, Mailman School of Public Health
Oversight for Human Research

• Office of Human Research Protection (OHRP)
  • [http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm)

• FDA

• New York State
OHRP

- Reviews institutional compliance with federal regulations governing the protection of human subjects in HHS-sponsored research (~30,000 protocols)
- Evaluates all written substantive allegations or indications of noncompliance with the HHS regulations
IRB Members

- At least five members, with varying backgrounds
- Sufficiently qualified through the experience, expertise and diversity of its members
- At least one member whose primary concerns are in scientific areas, whose primary concerns are in nonscientific areas, unaffiliated with institution
Criteria for Approval

- Risks to subjects are minimized
- Risks to subjects are reasonable in relation to anticipated benefits
- Selection of subjects is equitable
- Informed consent is sought and documented
- Adequate provision for monitoring data and protecting privacy/confidentiality
Required Elements of Informed Consent

• Statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental
Required Elements....

- Foreseeable risks or discomforts
- Benefits to the subject or to others
- Appropriate alternative procedures
- Extent to which confidentiality will be maintained
- Whether any compensation or treatments are available if injury occurs
- Whom to contact
- Statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits
Waiver of Consent

- The research involves no more than minimal risk to the subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The research could not practically be carried out without the waiver or alteration; and
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
Waiver of Documentation of Consent

• The only record linking the subject and research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality OR

• The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.
Additional Protections For...

- Pregnant Women, Human Fetuses and Neonates
- Prisoners
- Children
Examples of Exculpatory Language

• By agreeing to this use, you should understand that you will give up all claim to personal benefit from commercial or other use of these substances

• I waive any possibility of compensation for injuries that I may receive as a result of participation in this research
Examples of Acceptable Language

• By consenting to participate, you authorize the use of your bodily fluids and tissue samples for the research described above.

• This hospital is not able to offer financial compensation nor to absorb the costs of medical treatment should you be injured as a result of participating in this research.
Required Training--CUMC

- GCP
- HIPAA
- Research involving children
Certificate of Confidentiality

- So that researcher is not compelled in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings to identify research participants
- Issued by NIH (only after IRB approval)
Levels of IRB Review

- Full Board
- Expedited
- Exempt
Expedited Review

- Review by IRB Chair or a designated voting member or group of voting members, rather than by the entire IRB Committee. Federal rules permit expedited review for certain kinds of research involving no more than minimal risk and for minor changes in approved research.
Expeditable Criterion 1

• Clinical studies of drugs and medical devices when
  – Research on drugs for which an investigational new drug application (IND) is not required.
  – Research on medical devices for which (i) an investigational device exemption (IDE) is not required; or (ii) the medical device is cleared/approved for marketing and the device is being used in accordance with its cleared/approved labeling.
Expeditable Criteria 2-4

- Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture.
- Prospective collection of biological specimens for research purposes by noninvasive means.
- Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves.
Expeditable Criteria 5-7

• Research involving materials that have been collected, or will be collected solely for nonresearch purposes.
• Collection of data from voice, video, digital, or image recordings made for research purposes.
• Research on individual or group characteristics or behavior or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodology.
Expeditable Criterion 8

- Continuing review of research previously approved by the convened IRB as follows: (a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or (b) where no subjects have been enrolled and no additional risks have been identified; or (c) where the remaining research activities are limited to data analysis.
Expeditable Criterion 9

- Continuing review of research not conducted under an investigational new drug application or investigational device exemption where categories do not apply, but the IRB has documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.
Expeditable Criteria 10-12

- Minor change in previously approved research during the period (of one year or less) for which approval is authorized.
- Facilitative Review for Cooperative Amendment (CA/IAA)
- Administrative Review - Certain types of awards (e.g., program project and center grants) support multiple projects involving numerous investigators.
**Exempt Determination (IRB)**

- Research conducted in established or commonly accepted educational settings, involving normal educational practices or educational tests
- Study of existing data or specimens, if publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified
Exemptions

- Research conducted by or subject to approval of Department or Agency heads designed to study:
  (i) Public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.
- Taste and food quality evaluation and consumer acceptance studies
Other Review Processes

- Cancer Committee
- Radiation Safety Committee
- Conflict of Interest Committee
- Hazardous Materials Committee (even for blood draws)
- Stem cell research
- Prisoner research
- Individual departments (e.g. pediatrics)
- IRB is last to approve after all these!
HIPAA and Research

• Many researchers need to address the Privacy Standard of HIPAA
• This may require submission of authorization, waiver of authorization, or preparatory to research documents to the Privacy Board
• This is separate from IRB review
Investigational New Drug (IND)

- Application is filed with the FDA when a pharmacological agent is being tested for safety and effectiveness in humans or when an FDA approved drug is being used in a different dosage, for a different purpose, or in a different population than previously approved by the FDA.
Investigational Device Exemption (IDE)

- Mechanism by which new medical devices that could impose “significant risk” to subjects are tested
- IDE allows an investigational device to be used in a study to gather data on safety and efficacy (effectiveness) of the device.
- IDE is also required for an approved device which is being used off-label in a research study
Humanitarian Use Device (HUD)

- A designation given to devices that may benefit patients being treated for a disease that affects less than 4,000 individuals in the U.S. per year.
- Because device manufacturers may be less inclined to put resources towards devices for diseases in so few individuals, HUD provisions were created to provide greater access for the use of such devices.
Center for Drug Evaluation and Research

- [http://www.fda.gov/cder](http://www.fda.gov/cder)
- Largest of FDA's five centers, with a staff of about 1,800.
- Responsibility for both prescription and over-the-counter drugs.
- Investigational New Drug (IND) applications are administered by CDER
Center for Devices and Radiological Health

- [http://www.fda.gov/cdrh](http://www.fda.gov/cdrh)
- Oversees investigational device exemptions (IDE) and humanitarian device exemptions (HDE)
**Emergency Use Protocols**

- When there is need to use an investigational device in a manner inconsistent with the approved investigational plan or by a physician who is not part of the clinical study.

- Emergency use of an unapproved device may occur before an IDE is approved.
  - Life-threatening or serious disease or condition
  - No alternative
  - No time to obtain FDA approval
Compassionate use

- For patients who do not meet the requirements for inclusion in the clinical investigation but for whom the treating physician believes the device may provide a benefit in treating and/or diagnosing their disease or condition.
- Typically approved for individual patients but may be approved to treat a small group.
  - Serious disease or condition
  - No alternative
New York State Law

- No human research in the absence of the voluntary informed consent in writing by the human subject.
- For minors, consent in writing by the minor’s parent or legal guardian.
- For those legally unable to render consent, such consent shall be subscribed to in writing by such other person as may be legally empowered to act on behalf of the human subject.
What Kind of Review?

• Relationship between sleeping patterns and acting-out behavior in hospitalized psychiatric patients
• Effects of a new drug treatment for diabetic patients
• Cardiovascular effects of exercise following acute MI
• Comparison to two teaching methods for insertion of central lines
What Kind of Review

- Chart review of neurologic outcomes of patients following one type of neurosurgery
- Hormonal levels in normal women during the menstrual cycle
- Random digit dialing interviews in NYC to assess rates of influenza-type symptoms