Stony Brook University

FAR BEYOND

Overview of Human Subject Research

Human Subject Research

Objectives:

- Describe the three ethical principles and their application to research with humans
- Describe basic regulations related to research with humans
- Describe the process to submit applications to the Human Research Protection Program

Human Subject Research

What is research?

- As defined in the Code of Federal Regulations, research is:
  - A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge 45 CFR 46.102(d)

Human Subject Research

What is research?

- As defined in the Code of Federal Regulations, clinical investigation is:
  - Any experiment that involves a test article and one or more human subjects and that is subject to requirements for prior submission to the Food and Drug Administration (FDA).

21 CFR 50.3(c)

Human Subject Research

What is practice?

- Interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success (e.g., provide diagnosis, preventive treatment or therapy)

DHHS

Human Subject Research

What is practice?

- Even departing in a significant way from standard or accepted practice does not, in and of itself, constitute research. The fact that a procedure is new or untested does not automatically place it in the category of research.

DHHS

Human Subject Research

What is practice?

- Research and practice may be carried on together when research is designed to evaluate the safety and efficacy of a therapy. The general rule is…that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects.

DHHS

Human Subject Research

Is quality improvement research?

- Implement a practice to improve the quality of patient care
- Delivery of healthcare
- Measure and report provider performance data for clinic, practical, or administrative uses

DHHS

Human Subject Research

What is a human subject?

- A living individual about whom an investigator (whether professional or student) conducting research:
  (1) Obtains data information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens, or
  (2) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens

45 CFR 46.102(F)

Human Subject Research

What is a human subject?

- An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient.

21 CFR 50.3(g)

Human Subject Research

Intervention - includes both physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

Interaction includes communication or interpersonal contact between investigator and subject.

45 CFR 46.102(F)

Human Subject Research

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (for example, a medical record).

Private information is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information

45 CFR 46.102(F)

Human Subject Research

What is the Belmont Report?

- Respect for Persons: individuals should be treated as autonomous agents and persons with diminished autonomy are entitled to protection

DHHS

Human Subject Research

What is the Belmont Report?

- Beneficence: respecting the individual's decisions and protecting them from harm but also securing their well-being (e.g., maximize possible benefits and minimize possible harm)

DHHS

Human Subject Research

What is the Belmont Report?

- Justice: who receives the benefits of research and who bears its burdens

DHHS

Human Subject Research

Application of the Belmont Report

Respect	Acknowledge autonomy and protect those with diminished autonomy	Consent
Beneficence	Protect from harm and secure well-being	Risk/Benefit Analysis
Justice	Fairness in distribution (inclusion and exclusion criteria)	Subject Selection

Human Subject Research

Categorization of Research

- Exempt – no or low risk
- Expedite – “minimal risk”
- Full Committee – greater than minimal risk

DHHS

Human Subject Research

Minimal Risk

The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during performance of routine physical or psychological examinations or tests

DHHS

Human Subject Research

Informed Consent

Before involving a human subject in research, an investigator shall obtain the legally effective informed consent of the subject or the subject's LAR

- Provide information that a reasonable person would want to have in order to make an informed decision about whether to participate and an opportunity to discuss that information
- Facilitate the prospective subject's or legally authorized representative's understanding of the reasons why he/she would want to participate in the research
- Present "key information" that assists the prospective subject's understanding of the research (this is presented first in the consent form)

46.116(a)(4)

- Investigator or other designated individuals are responsible for…
  - Providing information when requested by the subject
  - Providing time and opportunity to discuss the research
  - Answering questions to improve the subjects' understanding
- If the research could be considered objectionable a robust description of the research is required

Key Information

46.116(a)(5)

- The Preamble of the Final Rule, lists a brief description of five "factors" (elements) at the beginning of an informed consent process that would encompass the "key information". These elements are…
  - Consent is being sought for research purposes and participation is voluntary
  - The purpose of the research, duration and procedures
  - Reasonably foreseeable risks/discomforts
  - Reasonably expected benefits
  - Appropriate alternative courses of treatment

Informed Consent

Consent Form

One of the following statements about any research that involves the **collection of identifiable private information or identifiable biospecimens**:

- A statement that **identifiers might be removed** from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens **could be used** for future research studies or distributed to another investigator for future research studies **without additional informed consent** from the subject or the legally authorized representative, if this might be a possibility; **or**
- A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, **will not be used or distributed** for future research studies.

Informed Consent

Consent Form

Applicable statements about any research that involves the **collection of identifiable private information or identifiable biospecimens should be inserted into the informed consent form:**

- A statement that 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;
- A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions;
- For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

Human Subject Research

Research Issues

- Recruitment materials are not included with the application (e.g., verbal recruitment scripts, emails, follow-up reminder notices, etc.)
- Consent forms submitted do not match the population of interest
- Questions left blank on the application
- Questionnaires, surveys, interview questions are not included

DHHS

Human Subject Research

Research Issues

- Study personnel not listed in application
- CITI training not up to date for all study personnel
- Protocols are not included
- Data Safety Monitoring Plans missing for studies that are greater than minimal risk
- Students submit their own studies rather than the faculty member
- Study not routed to the Department Head/Chair before it is submitted to the Human Research Protection Program

Practice of the IRB

New Study

- Submission of a study that uses surveys or questionnaires
  - Include the questionnaire or survey and think about the population with which it will be used
  - If the participants are children then parental permission and child assent is needed
  - If the participants are adults then a brief consent form is appropriate
  - Include recruitment materials (i.e., email, flyers, brochures)

Practice of the IRB

New Study

- Submission of a study that uses focus groups
  - Include the focus group questions that will be used
  - If the participants are children then parental permission and child assent is needed
  - If the participants are adults then an information sheet (or brief consent) is appropriate
  - Include recruitment materials (i.e., email, flyers, brochures)
  - If you are audio or videotaping, make sure it is mentioned in the consent/assent and that you cannot ensure confidentiality from other group members

Practice of the IRB

New Study

- Submission of a study that uses existing data
  - Include a list of the data elements you will be using in your study
  - Indicate if the data is anonymous or coded
  - Anonymous data is low to no risk and no consenting activity is needed
  - Coded data carries more risk
    - Request a waiver of informed consent/assent
    - Request a waiver of HIPPAA Authorization if the data is Protected Health Information

Practice of the IRB

New Study

- Submission of a study that includes an educational component
  - Include the educational component for the study (objectives, handouts, training material)
  - Indicate if the participants will be tested (pre and post)
  - Indicate if these individuals are employees or students (employees and students could be unduly influenced to participate)

Practice of the IRB

New Study

- Submission of a study that includes an educational component
  - Include how employees/students will be protected (from evaluations related to the study, employment, other benefits)
  - Can include a consent form that is not as lengthy but has all of the elements of informed consent
  - If the educational component is usual practice and the pre and post tests are anonymous, the study could be considered exempt
  - If pre and post tests will be coded, explain the coding system that will be used to link the two tests

Continuing Review

Regulations eliminated the requirement for continuing review for minimal risk studies unless an IRB reviewer determines otherwise. If the reviewer determines that the minimal risk study requires annual review, the reviewer must explicitly justify why it would enhance the protection of human subjects and document the determination.

Practice of the IRB

- What is continuing review?
  - During defined time intervals, it is the investigator's report about the study's progress and findings to date
  - It is a monitoring mechanism that assures continuing safeguards are in place to protect the rights and welfare of study participants
  - Provides an opportunity to revisit and reapply the ethical principles and norms outlined in the Belmont Report

Amdur & Bankert, 2002

Practice of the IRB

Continuing Review

- What if the project has expired?
  - When a project expires subject accrual must stop pending re-review by the IRB
  - Continuation of the intervention or interactions with subjects should stop unless it is in the best interest of the individual subject to continue (permission is needed from the IRB)

Amdur & Bankert, 2002

Practice of the IRB

Revisions to an Approved Protocol

- Types of revisions
  - Information revisions – changes in the protocol with no potential impact on the risks for human subjects
  - Minor revisions – changes in the protocol that may impact the research participants, but do not significantly affect the risks to the participants

Amdur & Bankert, 2002

Practice of the IRB

Revisions to an Approved Protocol

- Types of revisions
  - Major revisions
    - Minimal risk – the probability and magnitude of harm or discomfort anticipated in the research are not in and of themselves greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests
    - Major risk – involves more than minimal risk to research participants

Amdur & Bankert, 2002

Training Requirements

- Researchers and staff conducting research at Stony Brook University (whether behavioral or biomedical) are required to take the Collaborative Institutional Training Initiative (CITI) on line training
- The training can be accessed at www.citiprogram.org/
- The training is good for 3 years at which time a refresher course is offered

Training Requirements

- Researchers who predominately conduct research in biomedical area can take the CITI biomedical training and refresher courses
- Researchers who predominately conduct research in the behavioral area can take the CITI behavioral training and refresher courses
- Researchers who conduct both biomedical and behavioral can take both although there is some overlap. CITI takes that into account once the individual has finished one set of courses

Training Requirements

- Review core training documentation including the "Stony Brook University Standard Operating Policies and Procedures" and the "Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research"
- Be familiar with the University Human Research Protection Program website, and the availability of links and other information contained within

Office of Research Compliance

- Main office number:

  631-632-9036
- Email information:
  maryellen.herz@stonybrook.edu
- Address:

  Office of Research Compliance

  W5530 Melville Library

  Stony Brook University 11794-3368