UNIVERSITY of MARYLAND
SCHOOL OF NURSING

Demystifying the IRB process

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Disclosure

- The views expressed are mine and do not necessarily represent the views of the University of Maryland, Baltimore Human Research Protections Program.
- I have no conflicts of interest to declare.

Objectives

- Define human subjects research.
- Describe the Institutional Review Board (IRB) process.
- Learn how to complete an IRB submission.

Basic Ethical Principles

Belmont Report
1979

- **Respect for Persons**
  - Autonomy
  - Diminished autonomy entitled to protection
- **Beneficence**
  - Do no harm
  - Maximize benefits, minimize risk
- **Justice**
  - Fairness in distribution

Regulations and Guidelines

- Food and Drug Administration (21 CFR part 50 and 21 CFR part 56)
- Common Rule (45 CFR part 46)**
- International Council for Harmonisation, Good Clinical Practice (ICH GCP)

Common Rule

- The Common Rule (45 CFR part 46) is a federal policy regarding Human Subjects Protections that applies to Federal agencies and offices. The Common Rule includes requirements for assuring compliance, requirements for obtaining and documenting informed consent, and requirements for IRB review.
- Revisions went into effect January 21, 2019.

Revised common rule

- Purpose
  - Enhance human subjects protections
  - Reduce administrative burden
  - Align with current research climate
  - More flexibility

GCP

- International standard for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of studies.
- Provides assurance that the rights, safety, and welfare of human subjects is protected.
- Am I required to adhere to GCP? YES.

Definition

WHAT IS HUMAN SUBJECTS RESEARCH

Human Subjects Research

- Is this Research as defined by **DHHS** and involves Human Subjects as defined by **DHHS**
- Is this Research as defined by **FDA** and involves Human Subjects as defined by **FDA**

HRP-309 Worksheet- Human Research Determination
http://www.umaryland.edu/hrp/for-researchers/investigator-manual/referenced-materials

What is Research?

A **systematic investigation,** including research development, testing and evaluation, designed to develop or contribute to **generalizable** knowledge (45 CFR 46.102)

- **Is the activity an investigation?**
  Investigation: Searching inquiry for facts; detailed or careful examination
- **Is the investigation systematic?**
  Systematic: Having or involving a system, method, or plan
- **Is the systematic investigation designed to develop or contribute to knowledge?**
  Designed: evaluate whether the activities will develop or contribute to knowledge.
  Develop: to form the basis for a future contribution.
  Contribute: to result in.
  Knowledge: truths, facts, information
- **Is the knowledge the systematic investigation is designed to develop or contribute generalizable?**
  Generalizable: Universally or widely acceptable

If any are "No" the activity is NOT research under DHHS regulations

What is a Human Subject?

A living individual about whom an investigator conducting research**:**

(1) Obtains 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.

Not Research Examples

- Evidenced-Based Clinical Practice Guideline
- Quality Improvement
- Quality Assessment
- Classroom projects to fulfill course requirements
- Program Evaluations
- Public Health Practice
- Research on publically available data sets
- Case histories from a single patient
- Resource Utilization Review

Bankert, E. A., & Amdur, R. J. (2006). *Institutional review board : management and function*. Sudbury, Mass. : Jones and Bartlett, c2006

	Human Subject Research	Quality Improvement	Program Evaluation
Intent	• Develop or contribute to generalizable knowledge	• Improve a practice or process within a particular institution/setting	• To improve or evaluate a specific program
Design	• Develop or contribute to generalizable knowledge • May involve randomization	• Not designed to develop or contribute to generalizable knowledge • Does not involve randomization	• Not designed to develop or contribute to generalizable knowledge • Does not involved randomization • May involve comparisons of program
Motivation	• Occurs in large part as a result of individual professional goals and requirements	• Project occurs regardless of whether individuals conducting it may benefit professionally	• Project not initiated by the evaluator and occurs regardless of whether individuals conducting it may benefit professionally

Adapted from Cobb & Moberg, 2008

Case study 1

Determining Human Subjects Research

"Per the recommendations of the American Pediatric Association, physicians should be screening new mother's for post-partum depression (PPD). As part of their quality assurance activities the Bears Pediatric Center (BPC) reviewed records from 2016-2017 and noted that only 1/4th of mother's were screened for PPD. To improve the quality of care, we will be implementing an alert in the electronic medical record (EMR) at BPC to remind physicians to screen for PPD at every well-child visit up to one year of age. After 3 months of implementation, medical records will be reviewed to determine what percentage of mother's were asked about PPD. If the EMR alert is successful in reminding physicians it will remain part of the EMR system at BPC. This is a quality improvement project designed to improve patient care at BPC. It is not intended to be generalized to other settings and is intended solely for the improvement of patient care in this clinic. No identifying information will be recorded."

Is this research? Why or why not?

Case Study 2

Determining Human Subjects Research

- "We are designing a study to submit for grant funding examining contributors to why patients with a neurological condition don't engage in exercise despite literature showing beneficial effects. We plan to use a semi-structured interview to understand barriers to exercise. As we design the study, however, we need to make sure that the semi-structured interview that we're planning asks the correct questions and does so in meaningful ways. We also want to make sure the other measures used in the study reflect the issues that this population face. Thus, we would like to do two things: (1) attend a support group meeting (with their permission) to get their input on what barriers they experience to participating in exercise and (2) try the semi-structured interview with patients who are currently experiencing difficulties. These would be patients from an existing patient population in the Neurology outpatient clinic who are familiar with one of our treating physicians. It is estimated that the semi-structured interview will take 30-90 minutes to complete; the actual time will be noted as this will be important for study design. The interviews will be recorded for subsequent review and transcription but no identifiers will be transcribed. Up to 5 patients will be approached for this background information. This data is only being used to provide feedback to the investigator in order to assist with study design and grant preparation.

  We feel that these interviews may meet the criteria for Non Human Subjects Research at this stage as they are not designed to contribute to generalizable knowledge. The purpose of these interviews is to provide information necessary for the preparation of a research grant for a research protocol. Any subsequent research study would be submitted for IRB approval."
- Is this research? Why or why not?

Does my project require IRB review?

- Quality improvement, program evaluation or other projects that do not meet the definition of human subjects research or if you are unsure, should be submitted to the IRB for determination as an NHSR submission.
- Why?

What is CICERO?

Collaborative Institutional Comprehensive Evaluation of Research Online

- Comprehensive on-line system used to submit protocols for review to:
  - Institutional Review Board (IRB)
  - Institutional Animal Care and Use Committee (IACUC)
  - Institutional Biosafety Committee (IBC)
  - Radiation Safety Committee (RSC)
  - General Clinical Research Center (GCRC)
- Conditional Branching

Project Description

- What are you doing?
- How are you doing it?
- When are you doing your project?
- Where will you project take place?
- Who is involved?
- Why are you doing this project?
- Why you think your project is NHSR

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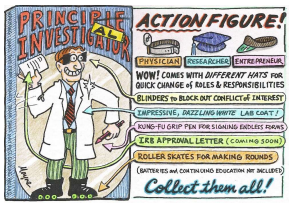
HUMAN SUBJECTS PROTECTIONS AND THE IRB

Who can be an investigator?



- Full-time *(>51% effort)* faculty member
- Professor, Associate Professor, Assistant Professor, ***or*** has otherwise been granted approval by the Institutional Official
- Investigators must be qualified by education, training, and experience

Investigator Responsibilities

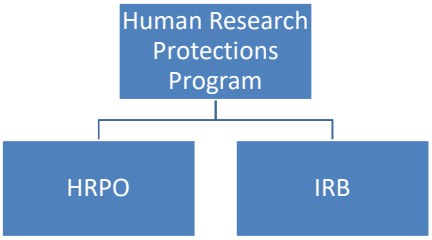
- Ultimately responsible for study conduct and ensuring the study is conducted in an ethical manner and consistent with all applicable policies and regulations.
- Assures there are adequate resources to conduct the study (staff, space, funding).
- Assures staff (direct and indirect reports) are appropriate trained.
- May delegate tasks to trained and qualified study staff.

http://ichgcp.net/4-investigator
http://www.umaryland.edu/hrp/for-researchers/investigator-manual/

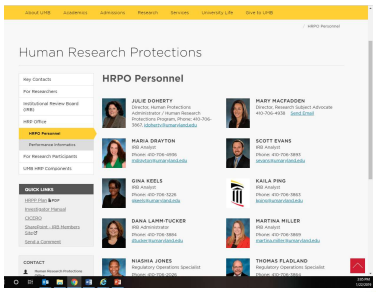
Training Requirements to Conduct Research at UMB

- **CITI Training (online)**
  - All individuals engaged in human subjects research at UMB are REQUIRED to complete CITI training (refresher every 3 years)
- **HIPAA Training (online)**
  - All individuals employed at UMB must take HIPAA 125
  - All individuals engaging in research at UMB must take HIPAA 201
- **<u>Additional</u> Requirements (online)**
  - Good Clinical Practice Training for NIH-funded studies OR studies conducted under the purview of UMSON

Human Subjects Protections at UMB



HRPO



Cartoon by Don Mayne www.researchcartoons.com

Institutional Review Board (IRB)

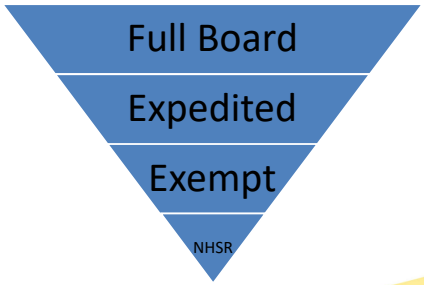
"An independent body constituted of medical, scientific, and non-scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial…" (ICH GCP 1.31)

- Composition of the IRB (ICH GCP 3.2.1)
  - At least 5 members
  - One member whose primary area of interest is nonscientific
  - One unaffiliated member

Risk Levels

- **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 the performance of routine physical or psychological examinations or tests. (45 CFR 46.102 i)
  - Chart reviews, surveys, physical exams, drawing blood or saliva sampling etc.
- **Greater than Minimal Risk**

Levels of Review



Exempt Research

- Exempt from the Common Rule.
- Under the new rule there are 8 categories of Exempt research.
- Must still follow UMB IRB Policies and Procedures.
- Cannot be FDA regulated.
- Some categories cannot involved children.
- Written informed consent versus information sheet

Examples

- Research in established or commonly accepted educational settings- cannot have adverse impacts of student learning
- Educational tests, surveys, interviews, observations of public behavior
- Benign behavioral interventions
- Secondary research with identifiable private information

Expedited Research

- No more than minimal risk to human subjects
- Fits into one of more the expedited categories
- Not reviewed by the fully convened IRB
- Examples of Expedited Research:
  - Blood draws
  - Biological samples (through noninvasive means)
  - Collection of data from voice, video, digital or image recordings
  - Survey, interviews, and focus groups
  - Behavioral interventions

http://www.hhs.gov/ohrp/policy/expedited98.html

Full Board Review

- Greater than Minimal Risk or not eligible for exempt or expedited review.
- The IRB may determine that a study requires full board review even if it appears to be eligible for exempt or expedited review.
- Reviews are conducted by the fully convened IRB.
- Decision is made by a majority of the assembled quorum.
- No member with a conflict of interest can participate in the decision .
- Drug studies, device studies, exercise studies.

Requirements for Approval

1. Risk(s) to participants are minimized
2. Risks to participants are reasonable in relation to the anticipated benefits and to the importance of the expected knowledge to be gained
   - Identify the risks associated with the research
   - Determine how risks are minimized
   - Identify probable benefits
   - Determine if the risks are reasonable in relation to the benefit to subject and the importance of the knowledge to be gained
   - Assure that potential subjects are provided with an accurate and fair description of the risks or discomforts and the anticipated benefits

www.hhs.gov/ohrp/archive/irb/irb_chapter3.htm
Institutional Review Board Guidebook, 1993

Requirements for Approval

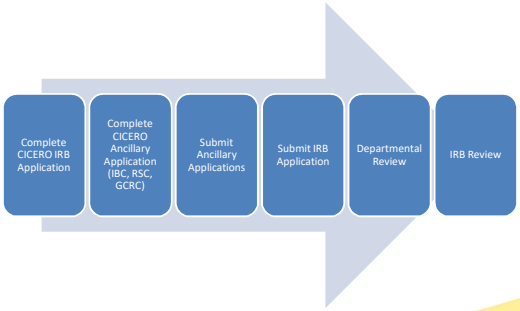
3. Equitable selection of participants
4. Informed consent will be obtained and the consent forms includes all required elements and is written in language that is understandable to the participants
5. Provisions for obtaining and documenting informed consent are appropriate
6. Privacy and confidentially are adequately protected
7. DSM Plan adequate
8. Additional safeguards are in place to protect the rights and welfare of vulnerable populations

www.hhs.gov/ohrp/archive/irb/irb_chapter3.htm
Institutional Review Board Guidebook, 1993

Submitting to the IRB

IRB SUBMISSION

Submission Process



Resources and Sites

- PI effort
- Availability of resources
- Study team member training
- Additional site approval

Justification, Objective and Research Design

- Clearly describe purpose and aims
- Consider if study design is appropriate to achieve objectives
- Describe qualitative or quantitative or both
- Explain the gaps in literature
- What scientific contribution will your study make?

Study Procedures

- "Recipe" for your study
- Recruitment → last study visit
- Who, what, where, when, why and how
- Include a study schedule

Study Schedule

Procedure	Baseline	Visit 1	Visit 2	Visit 3
Informed Consent and HIPAA	R			
Assess Inclusion/Exclusion	R			
Exercise Diary		R (daily)	R (daily)	R (daily)
EKG	C	R	R	R
Exercise Intervention	R	R	R	R
Exercise Survey	R			
Blood Sample	C	R	R	R

R = Research
C = Clinical

Sample Size and Data Analysis

- Highly recommend consulting with a statistician
- Provide a detailed power analysis
- Provide detailed plan for analysis for each study aim

Study Population

- Who are your study participants?
- Carefully consider your inclusion/exclusion criteria
- Can you feasibly recruit your identified population?
- Vulnerable populations
  - Persons with Diminished Decision-Making Capacity (cognitively impaired)
  - Students
  - Employees
  - Elderly
  - Critically ill
  - Economically or Educationally Disadvantaged

Data Collection

- How are you getting your data?
  - Medical record review
  - Surveys
  - Interviews
  - Observations
- Be specific
- Minimum necessary
- What kind of data are you collecting?
  - Anonymous
  - De-identified
  - Private

Confidentiality and Privacy

Privacy
is about the PERSON
- Refers to people
- Control
- What does the participant view as privacy

Confidentiality
is about the DATA

Examples?

Data Safety and Monitoring

- Commensurate with risk
- Levels
  - PI
  - Internal Committee
  - External Committee
  - Board

Recruitment

- Recruitment is a study procedure
- All recruitment methods must be approved
- Tailor recruitment methods to study population
  - Person-to-person
  - Flyers
  - Letters
  - Internet

HIPAA

- When does HIPAA apply?
- Do you need a HIPAA waiver?
  - Full waiver
  - Partial wavier

Risks and Benefits

- **What risks are associated with your study?**
  - Physical pain
  - Social/psychological/emotional, economic, legal risks, group stereotyping, embarrassment, stigma
- **How do we minimize risks?**
  - Appropriate study design
  - Training of all study staff
  - Conflicts of interest have been addressed
  - Only collect necessary data
  - Availability of medical or psychological resources
  - Proper management of data
  - De-identification
  - Appropriate expertise
  - Well-defined and appropriate eligibility criteria
  - Data safety and monitoring plan
- **Benefits**
  - Individual benefits versus societal benefits
  - Compensation is not a benefit

http://www.research.umn.edu/irb/download/EvaluatorsGuidetoIRB.pdf

Case Study 3
Evaluating Risk

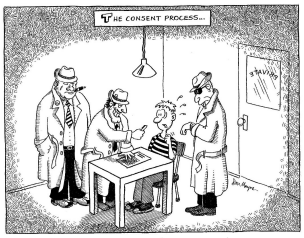
"The researcher wants to implement a mindfulness intervention to improve mental health outcomes of nurses working in high stress environments. Nurses at 5 different hospitals will participate in a 10 week mindfulness intervention. Study procedures include surveys to assess work satisfaction, depression, and anxiety symptoms. Surveys will be administered at pre-intervention, immediately post-intervention, and 30-days post-intervention. Basic demographics will be collected."

Potential Harms
- Confidentiality
- Employment status
- Suicidal ideation or intent to harm
- Negative emotional reactions

Minimize Risk
- Appropriate procedures for storing data
- Assign subject IDs
- Employer is unaware who is participating
- Plans in the event suicidal ideation or intent to harm is expressed
- Referral

Informed Consent

- Informed consent process
- Elements of informed consent
- Information Sheets versus Informed Consent Documents
- Waiver of Consent versus Waiver of Documentation of Consent
- Documentation of process
- Assessing understanding



Documents

- Protocol (if not using CICERO to build protocol)
- Assessments/Questionnaires
- Case Report Forms
- Investigator's Brochure/Package Insert
- Device Manuals
- Informed Consent Documents
- HIPAA Document
- Recruitment Material
- Advertisements
- Scripts (phone scripts, interview scripts)
- List of variables
- Study Schedule (with R & C designation)

Common Pitfalls

- Study procedures are not well described.
- The "type" of research isn't correctly identified in CICERO.
- Vulnerable populations are not considered.
- Risks to participants are not described.
- Procedures to minimize risks are not included.
- No sample size analysis or data analysis plan.
- Variables to be collected are not included.
- Informed consent document has errors, does not include elements of informed consent, is too complex.
- Inconsistency.

Common Pitfalls

- Does not adequately describe recruitment procedures and missing scripts or advertisements.
- Providing too much or too little information.
- Submitting before completion of CITI and HIPAA training or CITI training is expired.
- Inappropriate DSMP.
- Not including procedures to ensure participant understanding.
- Spelling, typos, grammatical errors (sloppy work).
- Cut, copy, paste from another protocol with incorrect information.

References

- http://www.umaryland.edu/hrp/for-researchers/investigator-manual/
- https://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-019.html
- http://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html
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