
Graduate Medical Education
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Overview

• Brief introduction to OHR and the IRB
• Determining engagement in human subjects research
• Ethical foundations
• IRB review types: emphasis on exempt and expedited review
• Researcher responsibilities
• Select Topics:
  • HIPAA and clinical research
  • Standard of Care vs. Research
  • CITI training
  • Common problems with submissions
  • Best ways to stay in compliance
GW Human Research Protection Program (HRPP)

• INSTITUTIONAL REVIEW BOARD (IRB):
  • Committee charged by the federal regulations and institutional policies with the oversight of human subjects research
  • Responsible for ensuring that the rights, welfare, and safety of human subjects are protected
  • Comprised of members across a variety of backgrounds

• OFFICE OF HUMAN RESEARCH (OHR):
  • Administrative support office for the IRB that assists the IRB in providing oversight for the protections of human subjects research conducted at GW
  • Pre-review all IRB application submissions and forms
  • Provide advice, guidance, and education on all aspects of IRB review and ethics
  • Monitoring
MAKING A DETERMINATION IF YOUR PROJECT REQUIRES IRB REVIEW AND APPROVAL
Question #1: Is it research?

- A *systematic investigation* designed to develop or contribute to *generalizable knowledge* (including research development, testing and evaluation) \(45 \text{ CFR 46.102(d)}\)
  
  - Systematized - Having or involving a system, method, or plan
  
  - Investigation - Testing an hypothesis and permitting conclusions to be drawn (i.e., detailed, careful examination)

  - Intended to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships)
    
    - Publishing or presenting the results at a conference
Question #2: Does the research involve human subjects

- A human subject is a living individual about whom an investigator conducting research obtains 45 CFR 46.102(f):
  - data through intervention or interaction with the individual; OR
  - identifiable private information
One notable exception: FDA-regulated research

- The U.S. Food and Drug Administration (FDA) regulations have different definitions for what is considered research and human subject:
  - Research = clinical investigation
  - Human subject = any recipient of a drug, device, or biologic as part of a clinical investigation, including healthy controls
- FDA regulations also have different investigator requirements/responsibilities
  - It is important that you:
    - Educate yourself on the pertinent regulations (21 CFR 312, 812, etc.)
    - Contact the IRB office and ask questions
    - Contact the FDA and ask questions
Test your Knowledge of the Definitions

- You are planning to do a secondary analysis and will present your findings at an upcoming conference. You will be given the following variables:
  - State
  - Gender
  - HIV status (positive/negative only)
  - Education level

- Are you conducting research?
- Is it human subjects research?
Ethical Foundations
Published by National Commission, 1979, the Belmont report was written with the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.

The Belmont Report established three basic ethical principles that are the cornerstone for regulations involving human subjects:

* Respect for Persons
* Beneficence
* Justice
Belmont Ethical Principles

**RESPECT FOR PERSONS:**
- Treat individuals as autonomous agents and provide additional protections for those with diminished autonomy
- Participation in research must be voluntary and informed (comprehended)

**INFORMED CONSENT PROCESS**

**BENEFICENCE:**
- “Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being”
- Avoid harm to the extent possible by minimizing risks and maximizing benefits
- Ensure that overall risks to study subjects do not outweigh the benefit to subject and to society

**MINIMIZATION OF RISKS**

**JUSTICE:**
- Selection of subjects is for reasons of science, related to the purpose of the study
- Fair distribution of benefits and burdens of research across society
- Equitable selection of subjects

**RECRUITMENT PROCESS & ELIGIBILITY CRITERIA**
Limit Autonomy = Vulnerable Populations

- Vulnerable populations are so-named because:
  - They are vulnerable to undue influence or coercion
    - Undue Influence = “…an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance”
    - Coercion = “…an overt threat of harm is intentionally presented by one person to another in order to obtain compliance.”
  - They have limited comprehension and understanding (i.e., children)

- The following groups are defined as vulnerable in the federal regulations:
  - Pregnant Women, Fetuses, & Neonates
  - Prisoners
  - Children

- Other groups to consider:
  - Patients
  - Cognitively impaired (older adults, mentally ill)
  - Educationally/economically disadvantaged
  - Employees/students
  - Military
Example: Patients are a Vulnerable Population…

- Who are susceptible to undue influence or coercion
- It is important to provide methods for patient participation to be truly voluntary. For example:
  - Have someone other than the treating physician obtaining consent
  - Use opt-in or opt-out “checkboxes” in lieu of signing a name, use drop-boxes, whenever possible
  - Do not present research information during stressful periods
Risks in Research

• Defining and Identifying Risks (CABLES) - Types of risk:
  – Cognitive/ Psychological
  – Affective
  – Biological/Physical
  – Legal
  – Economic/Financial
  – Social

• Risk Assessment
  – Evaluate the probability, frequency, magnitude of harm

• Plan to Minimize risks
  – Study is designed to minimize risks to subjects

• Monitoring risks
  – Risks to subjects are proactively monitored and minimized for the duration of the research
HUMAN SUBJECTS RESEARCH REVIEW: DETERMINING THE PATHWAY TO THE IRB
Categories of Review

- Risk Level
  - Risk determination involves the population being studied and the study procedures
  - Level of risk will dictate the review category

- Review Categories
  - Exempt: Less than minimal risk to the subjects
  - Expedited: Minimal risk to the subjects*
  - Full Board: Greater than minimal risk

- Minimal risk means that 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)].
Exempt Research

• Requires registration only prior to implementation
• Must meet one of the exempt research categories
  – Research in educational settings
  – Educational testing, surveys interviews or observation of public behavior
  – Research involving elected or public officials
  – Extension of Category 2 without the same level of oversight for the subject’s privacy
  – Research involving existing data (retrospective only)
  – Demonstration projects
  – Taste or food quality evaluation
Expedited Research

- Meets one or more of the expedited review categories and be no more than minimal risk

- May only be used where identification of the subjects and/or their responses would **not** reasonably place them that at risk for criminal or civil liability or be damaging* to the subjects, unless there are protections in place such that the risk is no greater than minimal
  * *Damaging = financial standing, employability, insurability, reputation, or be stigmatizing

- Research may involve **vulnerable populations**
Types of Studies that Might be Expedited

- Studies involving approved drugs or devices
- Studies involving a venipuncture
- Studies involving collection of biological specimens by non-invasive means (e.g., buccal swabs, saliva, hair or nail clippings, etc.)
- Studies involving collection of data through non-invasive means (e.g., using physical sensors, weighing, MRIs, ECGs, EEGs, ultrasounds, etc.)
- Data, documents, records or specimens collected or will be collected for non-research purposes (such as medical treatment, diagnosis, etc.)
- Data from voice, video, digital, or image recordings made for research purposes
Review Process

• For any category of human subjects research, the following process occurs:
  – Once a study is submitted in its entirety, it is assigned to an analyst for preliminary review.
  – The analyst will contact the PI and primary contact with questions and clarifications about the study.
  – Once satisfactory, the study is forwarded for formal review either by a member of the IRB or a designee. Formal review may result in additional questions.
  – Final approval is issued.
You are planning to conduct a chart review that involves collection of the following variables (data collection dates are: 01/01/2010 – 03/31/2011):

- Date of delivery
- Delivery complications
- Maternal date of birth

Is this study exempt or expedited?

You are planning to conduct an anonymous survey of patients in the infectious disease clinic. Subjects will be reporting on how, where/how they receive information about HIV/AIDS. You will be collecting age only.

Is this study exempt or expedited?
INVESTIGATOR RESPONSIBILITIES
Who is a Principal Investigator (PI)?

- The **Principal Investigator (PI)** is the *individual* who assumes *full responsibility* for a research project.

- At GW, the PI must be a full-time faculty member (with limited exceptions).

- One research team member should be designated as the “Principal Contact” for communication with the IRB.
PI Responsibilities

• Securing prior IRB review and approval for any nonexempt research, including any modifications to approved research
• Following any institutional policies and procedures
• Obtaining and documenting informed consent
• Ensuring that progress reports are submitted to the IRB IAW P&P and IRB determinations
• Ensuring prompt reporting of any unanticipated problems involving risks to subjects or others and any serious or continuing non-compliance
• Research record-keeping
SELECT TOPICS
When Does HIPAA Apply to Research?

• HIPAA applies to all covered entities (i.e., hospitals, practices, or providers) whenever you will be using health information for research purposes.
  – Health information is any information (oral or recorded) that is created or received by a health care provider and relates to the past, present, or future physical or mental health of an individual.
HIPAA Identifiers include:

- 18 elements that could be used to identify the individual, such as:
  - Names
  - Geographic subdivisions smaller than a state
  - All element of dates (DOB, DOS, DOA, DOD, etc.)
  - Telephone numbers
  - Email addresses
  - Social Security numbers
  - Medical record numbers
  - Health plan numbers
  - Account numbers
  - IP addresses
  - Voice or video
  - Full-face images
HIPAA and Clinical Research

- PHI may be used or disclosed for the purposes of the research if you obtain:
  - Full Authorization
    - Combined with the Informed Consent Document (ICD)
  - Partial Waiver of Authorization
    - Only reviewing the records to identify potential subjects for recruitment purposes
  - Full Waiver or Alteration of Authorization
    - Not practical to obtain (consent)
    - Obtaining signatures may present some risk (e.g., HIV, etc.)
- Note: HIPAA waiver review process concludes with the privacy officer **NOT** the IRB
Standard of Care vs. Research

• Be clear in the application what is the research and what is standard of care.

• Examples:
  – Two types of anti-hypertensives could be considered standard of care and the subject will be randomized to one of two types. The randomization is the research, not the drug.
  – A study looks at the effects of NSAIDs on women ages 40-50 focusing on ALTs specifically. Drawing blood for hepatotoxicity is normal for a patient with a history of prolonged use of NSAIDs, however you want an extra tube for specific ALT testing. The extra tube of blood is the research- not the standard of care LFTs.
CITI Training (www.citiprogram.org)

- All investigators and research team members who will interact with subjects or view identifiable information must complete human subjects protection training.
- CITI offers courses for biomedical and social behavioral investigators.
- CITI also offers courses for those who will be working with PHI called HIPS.
- To begin CITI training, you will need to:
  - Create a CITI account.
  - Register for the biomedical and HIPS courses. Note: these are different from the Responsible Conduct of Research modules.
  - Renew the CITI training every two years (biomedical only).
- If you have completed a similar training elsewhere, you can submit your certificate for review by the OHR.
Common Issues When Submitting to the IRB

- Planning…allow for enough time for the study to be reviewed and approved
- Incomplete submission packets (including signatures)
- Differentiating between standard of care versus research
- “Shortcutting” when completing the forms
- Inconsistencies across submission documents (protocol = application = consent form)
- Technical, lengthy consent forms
- Communication between PI and study team members
Best Ways to Stay in Compliance

- Submit IRB applications with enough time to review/approve
  - Consider your resources, including the time you have available;
  - Think through the study design, and
  - Plan for OHR/IRB questions!
- Submit modifications when changes to the research are needed *prior* to making this change
- Once the study is up and running, verify that you are compliant with the protocol as proposed to the IRB
- Submit renewal requests on time (i.e., within 30 days prior to expiration date)
  - Note: The expiration date is *not* a deadline
  - If the study is not renewed in time, stop all work (to include data analysis) until you receive approval from the IRB
  - If your renewal request is repeatedly late, this is non-compliance!
- Close your project before you leave GW!
Conclusion

• Remember that human subject protection is a partnership (we are in this together!); we all have roles and responsibilities to fulfill when conducting research
• Always be ethical in any research that you conduct
• Plan, plan, plan! (do not wait until the last minute)
• Keep the communication lines open with the OHR and IRB; this is the best method for ensuring a smooth, timely review and successful navigation of the review pathways
We Welcome Questions!!
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