

HRPO AND THE IRB

Ethical Design to Successful IRB Application

Abby Keeley
Manager, Compliance and Staff Education
akeeley@wustl.edu

Human subjects are essential to the conduct of research intended to improve human health.

The relationship between subjects and investigators should be founded on basic ethical principles: respect for persons, beneficence and justice.

The Belmont Report (1978)

- **Respect for Persons:**
Recognition of Autonomy
- **Beneficence:**
Balancing Risks and Benefits.
- **Justice:**
Equally Distributing Risks and Benefits



Criteria for IRB approval of research

Beneficence

1. Risks to Subjects are Minimized
2. Risks to Subjects are Reasonable in Relation to Anticipated Benefits

Justice

3. Selection of Subjects is Equitable

Respect for Persons

4. Informed Consent will be Sought
5. Informed Consent will be Appropriately Documented

Beneficence

6. Provision for Monitoring Data to Ensure Safety
7. Provision for Protecting Privacy and Confidentiality

Justice

8. Vulnerable Populations are Protected

Human Subject Regulation

US Health & Human Services
Office for Human Research Protections

- Research involving humans IF
 - Entity receives any federal funding for research AND
 - The entity is engaged in conducting the research
- Based on federal funding

US Food & Drug Administration

- Research involving humans IF
 - Biologics
 - Drugs
 - Devices
- NOT based on funding

Is it Human Subjects Research?

- Two parts (HHS regulations):
 - Research: A **systematic investigation**, including research development, testing, and evaluation, designed to develop or contribute to **generalizable knowledge**.

Is it Human Subjects Research?

- Two parts (HHS regulations):
 - Human Subject: a **living** individual **about whom** an investigator conducting research
 - Obtains information or biospecimens through intervention or interaction with the individual, and, uses, studies, or analyzes the information or biospecimens; or
 - Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Research or QA/QI: Key Considerations

| | Research | QI/QA |
|------------------|---|--|
| Purpose | To test a hypothesis | To assess or improve a process, program, or system OR to improve performance as judged by established/accepted standards |
| Starting point | To answer a question or test a hypothesis | To improve performance |
| Benefits | Knowledge sought may or may not benefit current subjects but may benefit future individuals | Knowledge sought directly benefits a process/program/system and may or may not directly benefit individuals |
| Risks/Burdens | May put subjects at risk | Does not increase risk to patients, with the exception of privacy/confidentiality concerns |
| Data Collection | Systematic data collection | Systematic data collection |
| End Point | Answer a research questions | Improve a program/process/system |
| Testing/Analysis | Statistically prove or disprove hypothesis | Compare a program/process/system to an established set of standards |

Research or QA/QI: Key Considerations

- Does the analytical or evaluative component of the activity change the way that the clinical care will be delivered in such a way that introduces or heightens risks to participants (may include randomization)?
- Is there funding from an external organization (E.g. National Science Foundation or National Institutes of Health) based on support of a “research paradigm” to carry out the proposed activity?
- Are participants randomized into different intervention groups in order to enhance confidence in differences that might be obscured by other selection methods?
- Does the project seek to test interventions that are beyond the scope of current science and experience, such as new treatments?
- Does the project involve care practices, interventions, or treatments that are not standard (neither consensus-based, nor evidence-based)?

Case Studies: Key Considerations

- A case study is a retrospective review of a single patient's clinical condition and/or treatment that does not include a hypothesis, data analysis or generalizable conclusions.
- A case series is a case study that uses information about 2-3 patients instead of one.
- Still HIPAA requirements for use of PHI
 - <https://hipaa.wustl.edu/contact/>
 - As a general rule, will require authorization of patient or legally authorized representative via Media Authorization Form
 - They may refer you to hospital HIPAA office if hospital based PHI

Case Studies: Key Considerations

- Case studies/series move into research when:
 - Interaction with the patient led you to develop a research question to further investigate.
 - This case compares or contrasts with other cases, leading to a comparative study of multiple cases.
 - Data collection is more extensive than under normal clinical practice. Such as ordering additional laboratory test or collecting additional data beyond that needed for clinical care
 - The intent is to publish an analytical report versus a descriptive review.

Is it Human Subjects Research?

- FDA

- Device: Subject means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control.
- Drug: A clinical investigation is any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects...any use of a drug **except for the use of a marketed drug in the course of medical practice**

FDA vs HHS: Biospecimens

In FDA world it doesn't matter whether it is identifiable or not –

Even “anonymous” specimens can fall under FDA human subjects regulations (& require IRB approval)

Human Subjects: Key Considerations

- Deceased individuals
 - IRB review is not required to use data and/or biospecimens taken from individuals for a primary purpose other than research.
 - IRB review is not required to use data and/or biospecimens taken from already deceased individuals for research purposes.
 - HIPAA requirements:
 - Use will be solely for research on the PHI of a decedent; and
 - The researcher has documentation of the death of the Individual about whom information is being sought, and
 - The PHI sought is necessary for the purposes of the

Human Subjects: Key Considerations

- Leftover Clinical Specimens
 - Identifiability of the specimen
 - Status of the individual (living or deceased)
 - Purpose of the research – Is it FDA regulated?
 - Status of the individual and identifiability of the specimen do not matter to the FDA.
- Secondary Use of Existing Research Specimens
 - Individual research studies and Repositories
 - Identifiability of the specimens
 - Coded with a key – This can be tricky and it depends
 - Study team cross-over
 - Purpose of the research – Is it FDA regulated?

Human Subjects: Key Considerations

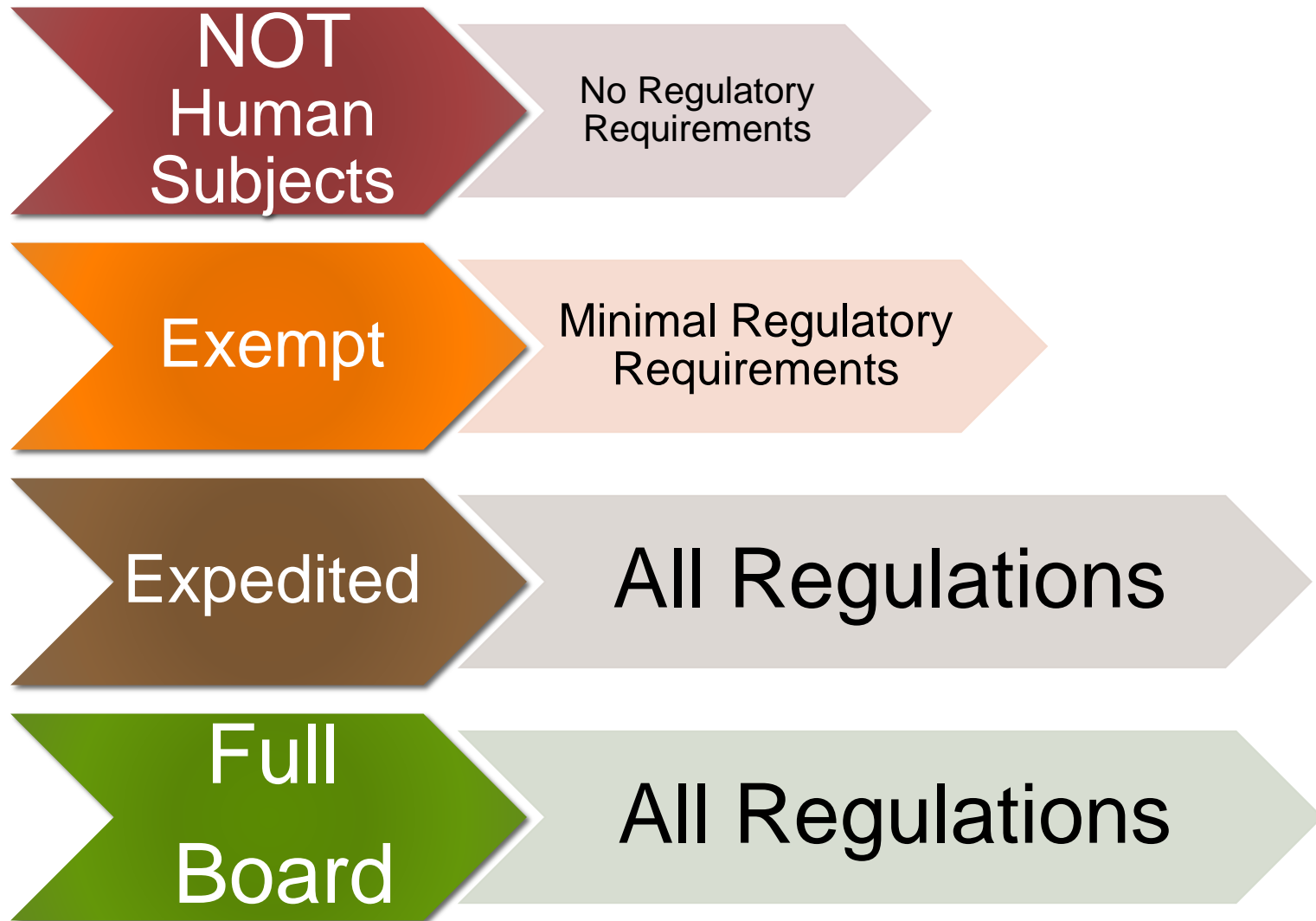
Existing data or specimens that are coded with a key/master list:

- For what purpose was the data/specimen originally collected?
- Who has access to the key/masterlist?
 - If this individual is not a member of the study team:
 - Is there an agreement or policy prohibiting release of the key/master list?
 - What is the individual's relationship to the project – are they an “investigator.”

Human Research or Not

- Use of tissue or specimens for internal QA purposes
 - Ex. Validating a test that is new to the lab—No
- Use of tissue or specimens to determine which laboratory test is more accurate—Yes
- Use of tissue or specimens obtained from autopsy—No, unless FDA regulated
- Case studies-most likely not

Not sure??—submit a non human request to IRB for official determination



Exempt Research

- Ex: Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:
 - The identifiable private information or identifiable biospecimens are publicly available
 - Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;
 - involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under HIPAA
- **Submit application to HRPO for Exempt determination**

Chart Reviews: Key Considerations

- What data are the minimal necessary?
 - Carefully selected inclusion/exclusion criteria to define your participants
 - Only propose what you need for data points and describe specifically what you need
 - “Medical history” – too broad
 - “Medical history related specifically to disease X - even more defined if possible
- Collection of identifiers
 - Make sure you include all identifiers needed to create the data set – not just those that are retained as part of the final data set

Chart Reviews: Key Considerations

- Data security
 - Paper – behind two locks
 - Electronic – on the secure server or on an encrypted device
- Source of data
 - Prior Studies
 - Provide the original source in the myIRB application
 - If the PI's are different we will require a letter of permission
 - Medical record data – additional permissions and documentation are required for PHI held by non WU/BJH/SLCH entities
 - EPIC – Ability to access does not mean you should access

Expedited Research

- Minimal risk AND fits into defined categories in regulations
- **Submit application to HRPO**
 - Screened/reviewed by “designated” reviewer
 - SAME review criteria as Full Board, only review is by single reviewer.
- **NO CONTINUING REVIEW REQUIRED!**

Full Board Review

- More than minimal risk OR does not fit Expedited categories
- Institutional Review Boards (IRBs – 2)
 - WU IRB
 - 6 meetings/week
 - ~180 members
 - Executive Chair + 7 Meeting Chairs
 - Protocol Adherence Review Committee (PARC)
 - 1/month
 - Dual role as HIPAA Privacy Board when Protected Health Information (PHI) is used or created for research

Waivers of Consent: Key Considerations

(1) The research involves no more than minimal risk to the subjects;

- This includes risks to privacy and confidentiality
- Genetic/genomic testing on “not previously consented” specimens will typically not be approved under a waiver

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

- Review text of consent forms for data/specimens coming from other studies

Waiver of Consent: Key Considerations

(3) The research could not practicably be carried out without the waiver or alteration;

- Often applied to retrospective data/specimens
- Can be applied to prospectively collected information with a compelling scientific justification
 - Avoid bias
 - Delayed consent

(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Obtaining Consent: Key Considerations

- Do not be overly restrictive when describing future research
 - The type of testing that can be done
 - The purposes related to the future research
- Be careful about making components optional
 - Anything that is optional brings the obligation to track and document
 - The only time future use and sharing cannot be mandatory is in research with a potential benefit

Genetic/Genomic Data: Key Considerations

- Consent forms should:
 - Include lay explanations of key terms (genes, DNA, RNA, genetic testing).
 - Address the scope of the planned testing (limited scope vs whole genome sequencing; creation of cell lines needs to be specifically discussed).
 - Describe the potential risks and protection against those risks.
 - Describe the potential for future use and sharing – do not be overly restrictive.
 - State whether incidental findings are a possibility and whether these results will be shared.
 - If either primary or incidental findings will be returned, the plan must be described to the participant within the consent form. Receiving these results should be optional, when possible.

NIH Genomic Data Sharing Policy

- Required to submit information in to dbGaP when creating large-scale genomic data with NIH funds
- Large-scale genomic data include genome-wide association studies (GWAS), single nucleotide polymorphisms (SNP) arrays, and genome sequence, transcriptomic, metagenomic, epigenomic, and gene expression data.

NIH Genomic Data Sharing Policy

- Should obtain consent to share genetic data
- Samples collected prior to effective date of policy, January 25, 2015, may submit data without consent at institution's discretion
- Samples collected after the effective date
 - Compelling scientific reasons that necessitate the use of genomic data
 - investigators should provide a justification in the funding request for their use. NIH will review the justification and decide whether to make an exception

Alternate sources of specimens

- Collection of blood, urine, or other specimens from employees or students who are subordinate to the PI (or another research team member)
 - This is allowed as long as you are not targeting these individuals
 - Must request permission to include these individuals in myIRB section 2
 - myIRB 1.12 should address recruitment and consent process associated with these individuals

Resources

HRPO Help Services

- SWAT On-Call
- Office Hours
- IRB Consultations

More Information...

- [IRB Policy Document](#)
- [Research Guide](#)
- i-button help text within myIRB application