Office for Human Research Protections (OHRP)
Webinar Series
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When PI's Come A-Knockin':

Everything Investigators Want to Know but are Afraid to Ask

Michelle Feige, MSW
Division of Education & Development (DED)
Office for Human Research Protections (OHRP)
Department of Health and Human Services (HHS)

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Poll

How much research experience have you had as a PI?

a) one year or less
b) 1-5 years
c) 6-10 years
d) Over 10 years
e) I am not a PI

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Poll

I have a good working relationship with my IRB?

a) Very true
b) Somewhat true
c) Not at all true
d) N/A

Outline

- Background & Overview
- Investigator Responsibilities
  - Regulations –what & when?
  - Roles & responsibilities
  - Informed consent/waivers
  - Incident reporting
- Contact Information

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What *is* the Office for Human Research Protections (OHRP) and Why Should I Care?

- **Provides leadership in protection of rights, welfare, and wellbeing of subjects involved in research conducted or supported by US Department of Health and Human Services**
- **Provides clarification and guidance**
- **Develops educational programs and materials**
- **Maintains regulatory oversight**
- **Provides advice on ethical and regulatory issues pertaining to biomedical and behavioral research**

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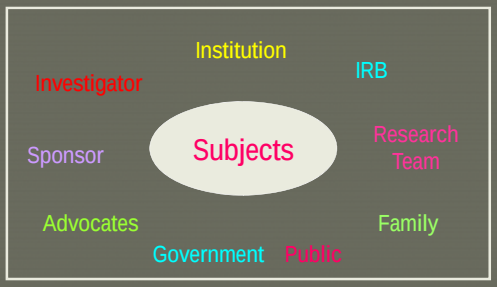
Who is Responsible for Protecting Human Subjects?

It's is a Shared Responsibility



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Who are "Investigators"?

Investigators are…

"an individual performing various tasks related to the conduct of human subjects research activities, such as obtaining informed consent from subjects, interacting with subjects, and communicating with the IRB."

…See FAQ's on Investigator Responsibilities

What are my Responsibilities as an Investigator?

Conduct Ethical Research

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The Belmont Report

Ethical Principles and Guidelines for the Protection of Human Subjects of Research

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
April 18, 1979

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The Belmont Report

- Beneficence
- Justice
- Respect for Persons

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What are my Responsibilities as an Investigator?

Follow the Rules

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Regulation for the Protection of Human Subjects

HHS regulations: 45 CFR part 46 and all subparts

Subpart A – basic HHS Policy - "The Common Rule"
or Federal Policy
- Other federal departments & agencies have adopted

Departments of Agriculture, Energy, Commerce, HUD, Justice, Defense, Education, Veterans Affairs, Transportation, HHS, & Home land Security. NSF, NASA, EPA, AID, CIA, and the Consumer Product Safety Commission

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Additional 45 CFR part 46 Protections

- **Subpart B** - Pregnant Women, Human Fetuses, and Neonates
- **Subpart C** - Prisoners
- **Subpart D** – Children
- **Subpart E-** IRB Registration

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Other Regulatory Entities…

- FDA Regulations
- Other Dept/Agencies
- State and Local Laws
- Institutional Policies

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How do I know when the Regulations Apply?

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The Regulations Apply when:

- Research involving human subjects conducted or supported by HHS that is not otherwise exempt

-OR-

- Non-exempt human subject research covered by Assurance of Compliance

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Do the Regulations Apply?

1. Does activity involve *Research*?
2. Does research involve *Human Subjects*?
3. Is human subjects research *Exempt*?

ASK QUESTIONS IN **THIS ORDER**!

Human Subject Regulations Decision Chart:
http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html

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Does the Activity Involve Research?

- Research – a **systematic investigation** designed to develop or contribute to **generalizable knowledge**
  - includes research development, testing, evaluation, pilot studies

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Pre-test poll

Human Subjects are involved in my research when I obtain:

a) identifiable private information about a subject
b) data through an intervention with a subject
c) identifiable private information about a deceased subject
d) A & B

Does the Research Involve Human Subjects?

- Human subject – a living individual about whom an investigator conducting research obtains
  - data through intervention or interaction with the individual, or
  - identifiable private information*

* Identity of the subject is or may readily be ascertained by the investigator or associated with the information

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Is the Human Subject Research Exempt?
Categories of Exempt Research*

1. Normal educational practices in established educational settings
2. Educational tests, surveys, interviews, or observation of public behavior -unless identified & sensitive**
3. Research on elected or appointed public officials or candidates for public office or protecting confidentiality without exception
4. Research using existing data, if publicly available or recorded without identifiers
5. Evaluation of public benefit service programs
6. Taste and food quality evaluation and consumer acceptance studies

§ 46.101(b)(1-6)

* Exception for prisoners
** Exception for children

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Where Can I Find Help?

- Human Subject Regulations Decision Charts
  http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html
- FAQs on Quality Improvement Activities
  http://answers.hhs.gov/ohrp/categories/1569
- Guidance on Engagement in Human Subjects Research
  http://www.hhs.gov/ohrp/policy/engage08.html

CALL US!

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So now I know that the regs apply to my research activities… what is my next step?

Understand and follow:

- *the HHS regulations*
- *IRB & institutional policies and procedures*

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Poll

When do I need to obtain IRB review and approval?

(a) prior to involving subjects in research activities
(b) at least annually
(c) prior to initiating any changes to approved research
(d) all of the above

When do I need to get IRB review and approval?

Obtain IRB review and approval for non-exempt human subjects research
(a) prior to involving subjects (initial review)
(b) at least annually (continuing review), and
(c) prior to initiating any changes to approved research.

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What are the types of IRB Review?

- Convened meeting of IRB
- Expedited review
  - minor changes to approved research
  - no greater than minimal risk and on "list" at:

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

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Help your IRB to help YOU!

§ 46.109, 46.111 & 46.116

Criteria for IRB Approval

Findings at §46.111

- risks minimized
- risk/benefit ratio reasonable
- subject selection equitable
- informed consent-obtained & documented
- data monitored
- privacy and confidentiality
- vulnerable populations: safeguards

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Considerations for IRB Review and Approval

- Understand IRB expectations and policies
- Provide sufficient information and materials
- Recognize and manage conflicts of interest
  - (e.g., disclose, reduce, eliminate)
- Comply with IRB decisions and requirements
- Respond to IRB requests in a timely fashion

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Continuing Review

An IRB must conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year

§ 45 CFR 46.109(e).

At the time of continuing review, what should I provide to the IRB?

Follow your institution's SOPs and report progress of approved research to the IRB, as often and in the manner prescribed by the IRB

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Progress Report might include:

- Number of subjects accrued
- Unanticipated problems (or adverse events)
- Withdrawal of subjects
- Complaints about the research
- Summary of any recent literature, findings, or other relevant information, especially information about risks associated with the research
- Copy of the current informed consent document
- Amendments or modifications

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What do I need to know about informed consent?

Do I need to obtain and document informed consent?

Unless waived by the IRB, YES!

YES!

If you are conducting non-exempt human subjects research, unless waived or altered, you must obtain and document legally effective informed consent, assent, and parental permission in accord with §46.116 and applicable subpart(s) and as approved by the IRB.

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What information needs to be in the consent form?

Informed Consent

Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by §46.116

§ 46.111(a)(4)

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Basic Elements of Informed Consent

- Research
  - Purpose
  - Duration
  - Procedures
- Risks/discomforts
- Benefits
- Alternatives
- Confidentiality
- Compensation for injury
- Whom to contact
- Right to refuse or withdraw

§46.116(a)

Additional elements at §46.116(b), when appropriate

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Are there times I don't need to obtain consent?

Informed Consent – Waiver OR Alteration at §46.116(d)

Waiver may be of some or all of the required elements, or of requirement for consent *in toto*

If IRB finds and documents that:

- no greater than minimal risk,
- will not adversely affect rights & welfare of subjects,
- research could not practicably be carried out without the waiver or alteration, AND
- when appropriate, subjects will be "debriefed" after participation

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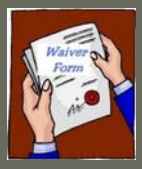
Emergency research waiver of consent

- For limited class of research in emergency settings, both FDA and OHRP have waived general requirement for informed consent if certain conditions are met.
- OHRP guidance on emergency waiver: http://www.hhs.gov/ohrp/policy/hsdc97-01.html

*Are there times when I don't need to **document** informed consent?*



Waiver Written Documentation – Informed Consent - §46.117(c)

IRB may waive documentation if it finds either:

1. consent form only record linking subject and research; *AND* principal risk from breach of confidentiality

OR

2 minimal risk research; *AND* involves no procedures for which written consent is normally required outside of the research context

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When obtaining consent from subjects (or their LAR's), what should I be aware of?

The Consent Process

- Informed consent is an ongoing process
- Educational process between investigator and prospective subject.
- Update consent form as appropriate/mandated by IRB
- Provide copy to subject or LAR
- Subpart D –
  - Child assent
  - Parental or guardian permission

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The Consent Process

The key elements of the consent process include:

- **full disclosure** of the nature of the research and the subject's participation
- **facilitate understanding** on the part of the potential subjects
- the subject's **voluntary** choice to participate

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After consent is obtained, how do I ensure ongoing protections during a research study?

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Considerations for Ongoing Protections

- Ensure informed consent is preserved
- Assure privacy and confidentiality
- Monitor rights and welfare of subjects
- Submit timely continuing review application
- Safety monitoring
- Report incidents
- Added safeguards for vulnerable populations

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What are my Responsibilities for Reporting "Incidents"?

OHRP Reporting Requirements

- Unanticipated Problems Involving Risks to Subjects or Others
- Serious or Continuing Noncompliance with the Regulations or IRB Requirements
- Suspension or Termination of IRB Approval

§ 46.103(b)(5)

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What is an *adverse event*?

- **Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research**
- **AEs encompass both physical and psychological harms**
- **AEs occur most commonly in the context of biomedical research, *although on occasion, they can occur in the context of social and behavioral research***

What is an Unanticipated Problem?

Incident, experience, or outcome that is:

- Unexpected (nature, severity, frequency)
- Related or possibly related to research, AND
- Suggests greater risk of harm than previously known or recognized

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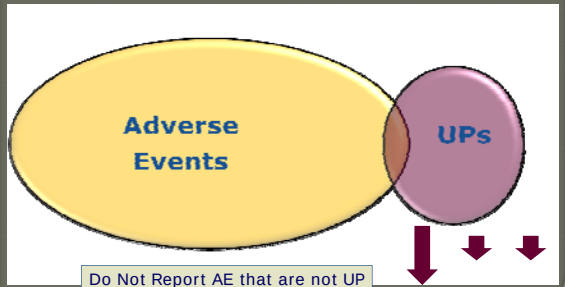
Most Adverse Events are not Unanticipated Problems



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What are my responsibilities once the study is completed?

What are my responsibilities once the study is completed?

- Follow institution's policies regarding notification to IRB that study is completed
- Retain signed consent documents and other records as required by the IRB or institution (see your institution's SOPs)
  - For at least three years past completion of the research
  - Accessible for inspection and copying
  - In accord with institutional policies & other regulations
- Store study data consistent with IRB plan
- Honor commitments
  - Provide information and compensation to subjects
  - Protect the privacy of subjects & confidentiality of data

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Key Points:

- Follow Belmont Report, federal regulations, IRB & institutional procedures and policies
- Obtain, document, and retain legally effective informed consent
- Report changes to the IRB
- Ensure ongoing protections
- Understand role when reporting incidents to OHRP

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Contact Information

OHRP website: http://www.hhs.gov/ohrp/

OHRP telephone: 240-453-6900 or

toll free:1-866-447-4777

OHRP e-mail: ohrp@hhs.gov

JOIN THE OHRP LISTSERV!

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