Noncompliance, Unanticipated Problems & Complaints

Presented by Jason Malone, MPH

3:25pm-4:25pm

UW Husky Union Building

Noncompliance, Unanticipated Problems & Complaints:

Learn to Prevent, Correct and Report

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Learning Objectives

By the end of this session, you will be able to:

- Discuss the roles and responsibilities related to reporting new information
- Describe the who, what and why for reporting new information
- Describe the framework for developing a corrective and preventive action plan in response to an event
- Identify processes to set studies up for success in order to prevent unanticipated problems and non-compliance

Framework

Initial Application

- Known Risks
- Theoretical Risks
- Everything will be conducted exactly as described in IRB application/study protocol

RNI = Report of New Information

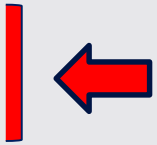
- Known or Theoretical Risks Happen
  - AND are reportable (e.g. occur at greater frequency, severity, nature than anticipated)
- Unknown/Unexpected Risks Happen (related, reportable)
- Things don't go according to plan (e.g. noncompliance with study protocol)
- Other New Information (e.g. revised IB, publication)

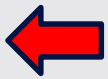
What to Report?

What needs to be reported? The regs say:

- 45 CFR 46.108(a)(3) *Establish and follow written procedures for:… (iii) ensuring prompt reporting to the IRB of proposed changes in a research activity…* [21 CFR 56.108(a)(3)]
- 45 CFR 46.108(a)(4) *Establish and follow written procedures for ensuring prompt reporting to the IRB; appropriate institutional officials; the department or agency head; and the Office for Human Research Protections, HHS, or any successor office, or the equivalent office within the appropriate Federal department or agency of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB;* [21 CFR 56.108(b)]
- 45 CFR 46.116(b)(5) Additional Elements of Informed Consent - *A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject* [21 CFR 50.25(b)(5)]

Information or Event	When to report
Qualifying Medical problem covered by UW HSAP	Report within 24 hours
Breach (or risk of breach) or loss of subject confidentiality or privacy	
Inappropriate access or use of protected health information (PHI)	
Incidental incarceration of a research subject in a study that the IRB has not approved for the inclusion of prisoners and where study activities or data collection will continue while the subject is incarcerated.	Report within 3 business days
For DOD funded EFIC studies only: All incidental incarceration of a research subject even if study activities and data collection will not occur during the incarceration	
Unanticipated problem	Report within 10 business days
Unanticipated adverse device effect	
Serious non-compliance	
Continuing non-compliance	
Emergency deviation from IRB-approved procedures made without prior IRB review to eliminate an apparent immediate hazard to a subject or others	
Continuation of research after IRB approval has lapsed, because the procedures are of direct benefit to the individual subjects or withholding the research intervention (if any) may increase risks to subjects	
Complaint from a subject or person about the study, which cannot be resolved by the study team	
Audit, inspection, compliance or safety-related inquiry from a federal agency	
Information that indicates a new or increased risk or safety issue (or a decrease in study benefits) (e.g. revised IB, package insert, or device manual; changes to FDA-approved labeling, restrictions, or warnings)	
Premature suspension or termination of some or all of the research by the sponsor, researcher, or institution	
Data Safety Monitoring Board (DSMB) or other study monitoring reports	
Change in credentialing, licensing, resources, or facilities that affect the research	





What to Report - Unanticipated Problem

Any incident, experience, or outcome that meets all of the following criteria:

- Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized

OHRP Unanticipated Problems Involving Risks & Adverse Events Guidance (2007)

What to Report - Unanticipated Adverse Device Effect

- Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

21 CFR 812.3(s) Unanticipated adverse device effect

What to Report - Noncompliance

An action or omission on the part of the researcher that is inconsistent with any of the following:

- The ethical principles of human subjects research as described in the Belmont Report;
- Federal, state, and/or local regulations applicable to human subjects research under the jurisdiction of the UW IRB;
- UW policies and procedures governing human subjects research;
- The research activities as approved by the UW IRB, including any IRB requirements or determinations.

What to Report - Serious Noncompliance

Non-compliance which meets any of the following criteria:

- Significant increase of the risks to, or jeopardizes the safety, welfare, and/or rights of, one or more subjects or others;
- Significant decrease of the potential benefits;
- Compromises the scientific integrity of a study such that important conclusions can no longer be reached.

What to Report - Continuing Noncompliance

A pattern of repeated non-compliance by the same investigator or the IRB that meets any of the following criteria:

- Suggests the likelihood that non-compliance will continue without intervention;
- Represents a failure to respond to a request to resolve an episode of non-compliance or a pattern of minor non-compliance;
- Increases the potential for serious non-compliance

I have been repeating the same mistakes in life for so long now, I may as well call them traditions.

What to Report - Research Complaint

- Complaints or concerns about UW research from a potential, past or current research subject (or the subject's representative), or

- Concerns about the conduct of UW research from a research staff member or any other concerned person or organization.

Why Do You Need to Report?

We ask for and review RNI so that we can:

- Meet regulatory obligations
  - Researchers must report Changes in research activity, Unanticipated problems, Serious NC, Continuing NC, provide new findings to subjects
  - IRB must assess and make determinations of UAP, SNC, CNC
- Facilitate Federal and Institutional Reporting (i.e. breach notifications and loss of confidentiality to UW Medicine Compliance, UW Privacy Office)
- Ensure the immediate problem has been addressed
- Ensure any proposed corrective action plan (CAP) will prevent future problems
- Ensure the risk level of the study is still appropriate
- Ensure the study continues to meet the criteria for approval

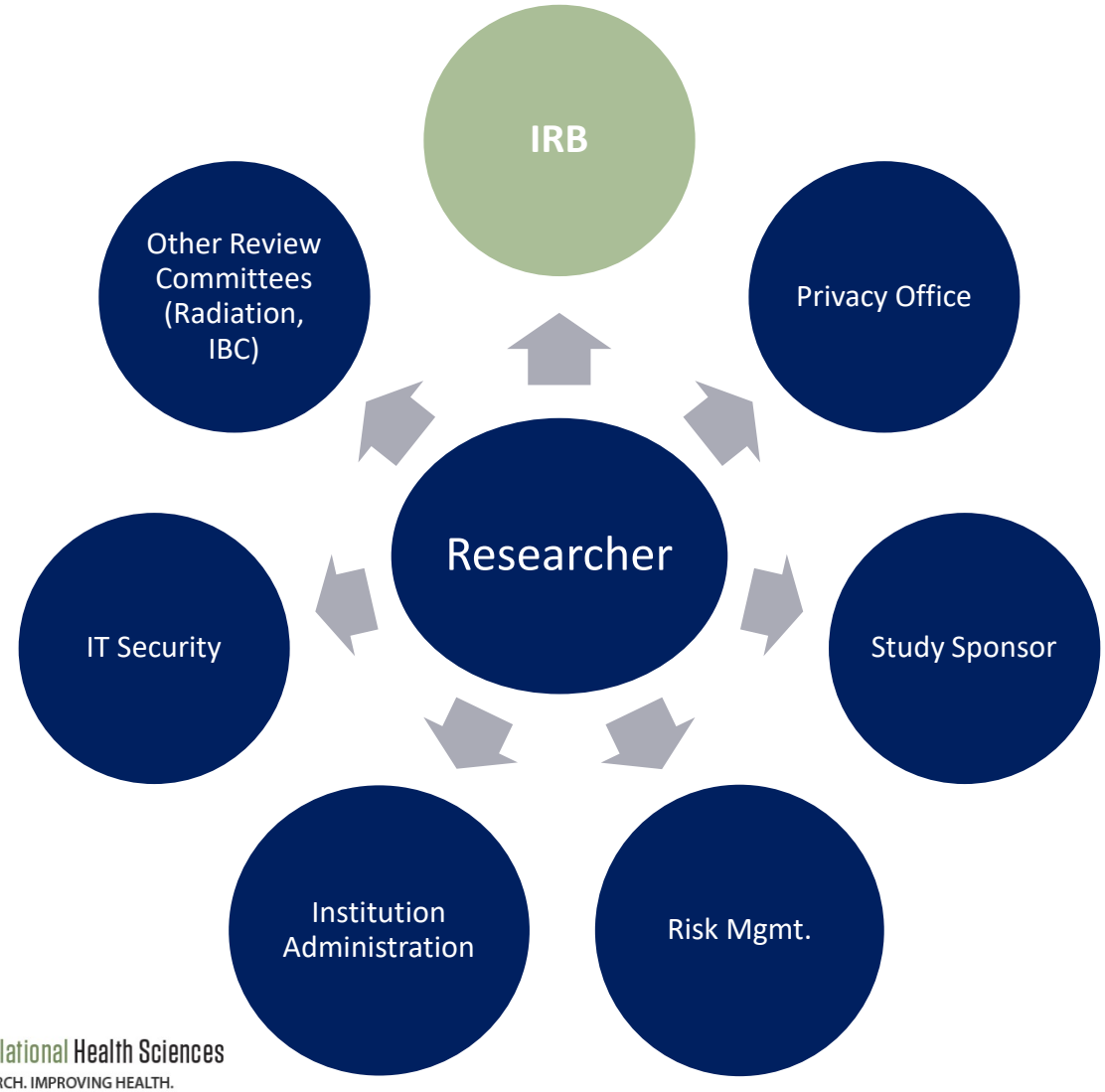
How to Report

- Follow your institution's procedures and use their required forms
- Ensure you've done a root cause analysis of the problem
- Propose appropriate solutions
- Consider using the S.M.A.R.T. approach
  - **S**pecific
  - **M**easureable
  - **A**chievable
  - **R**ealistic
  - **T**ime-bound

Corrective Action Plan (CAP) - SMART

- **S**pecific: Compliant with regulations, addresses the full observation or root cause, accountable to named individual or role
- **M**easurable: Action can be measured to demonstrate whether it is adequate to address the root cause
- **A**chievable: Addresses all implicated processes and levels
- **R**ealistic: Plan can be carried out given available resources, knowledge and expertise
- **T**ime-bound: Assigned to a person or role who can accomplish the action in a given time period, addresses urgency and criticality

Other Reporting



When to Report

- Reporting timelines vary from institution to institution and in some instances depend on the nature of the event
  - Example – UW
    - 24 hours: Breach, loss of confidentiality, inappropriate access/use of PHI
    - 3 business days – incarceration of a study subject
    - 10 business days – everything else
  - Example – Seattle Children's
    - 5 business days for everything
- It is your responsibility to know when to report and to do so in a timely fashion

Available Resources

- UW Reporting New Information - https://www.washington.edu/research/hsd/study-activities/report-events-and-new-information/
- Seattle Children's Reporting New Information - https://www.seattlechildrens.org/globalassets/documents/research/irb/click/reporting-new-information-2018.pdf
- Fred Hutch - https://extranet.fredhutch.org/en/u/irb/policies-and-procedures/_jcr_content/leftParsys/download_29/file.res/IRB-Reporting-Obligations-PIs-Policy.pdf
- WIRB Promptly Reportable Information - https://www.wirb.com/Documents/PRI.pdf

How to Avoid Reportable Events

"A clever person solves a problem.
A wise person avoids it."
-Albert Einstein

How to Avoid Reportable Events

Unanticipated Problems/Adverse Device Effects

- Adequately assess all known and possible risks
  - Literature review
  - Expert clinical assessment
- Outline risks in the consent form
- Incorporate adequate safeguards in study design to mitigate risk
- Have an effective data and safety monitoring plan
  - Routine collection and review of AEs
  - Independent monitoring where appropriate (medical monitor, Data & Safety Monitoring Board)

How to Avoid Reportable Events

Noncompliance

- Study design
  - Realistic (e.g. both subjects and study staff can follow)
  - Flexible where appropriate
- Case Report Forms
  - Match current protocol (i.e. capture only data outlined in protocol and IRB application)
    - Updated as modifications occur
  - Avoid unnecessary subject identifiers
  - Avoid duplicative data capture (e.g. paper forms and REDCap)

How to Avoid Reportable Events

Noncompliance continued…

- Training
  - Study Staff
  - Collaborators
- Communication
  - Frequency & methodology
  - Inclusive of entire research team and non-research collaborators
  - Address multi-site collaborations (if applicable)
- Quality Assurance
  - Appropriate ‘check steps’

How to Avoid Reportable Events

Subject Complaints

- Set Reasonable Expectations
- Be Clear in Your Communications
  - Recruitment
  - Consent Form
  - Study Materials
- Be Responsive
  - Subjects know who and how to contact research team
  - Inquiries returned in a timely fashion
- Honor your commitments
  - Compensation
  - Return of results

Available Resources

Don’t reinvent the wheel!

- Many institutions have templates (e.g. study protocol, case report forms) you can use
  - ITHS Study Document Templates - https://www.iths.org/investigators/forms-templates/study-document-templates/
- Consultations
  - Mentor/Experienced colleague
  - IRB Office

Case Studies - Questions

1. Is this a reportable event to the IRB?
2. Are there other offices this should be reported to?
3. What's the root cause of the event?
4. How would you solve the immediate problem?
5. What would you do to prevent the problem from occurring in the future (SMART)?
6. What could have been done to prevent the problem in the first place?