THE OHIO STATE UNIVERSITY

Event Reporting in Human Subjects Research

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Session Objectives

- Overview of the Revised Event Reporting Policy
- What, When & How to Report
- IRB Reporting Requirements
- Case Studies

2016 Policy Revision Initiative

- Revise and edit 39 existing policies
- Regulatory inventory
- AAHRPP standards
- Institutional interpretation (Ohio State vs peers)
- Process improvement opportunities
- Best practices

Event Reporting - Goal of Revision

- Clarify policy & provide better guidance
- Reduce administrative burden for researchers, IRBs, ORRP staff, sponsors & regulatory agencies
- Provide case examples
- Provide additional education
- Align Buck-IRB application with policy

Event Reporting - Revision Process

- Identify the regulations & guidance documents
- Collaborate with key research entities
  - Opportunity to clarify reporting responsibilities
  - Assess educational needs
- Trends for over/under reporting
- Identify IRB, PI & sponsor responsibilities
- Identify administration inefficiencies

Department of Health & Human Services (DHHS)

- Office for Human Research Protections (OHRP)
  - 45 CFR 46
- Food & Drug Administration (FDA)
  - 21 CFR 50
  - 21 CFR 56
  - 21 CFR 312
  - 21 CFR 812

Defines Roles and Responsibilities of
Principal Investigator, Sponsor & IRB

Routine Reporting

- Continuing Review
  - Annual Review
  - Annual Status Report
- Amendments
  - Change in Research
  - Change in Personnel
  - Change in Funding
- Final Study Report

Prompt Reporting

- Unanticipated Problems Involving Risks to Subjects or Others (UPIRSO)
- Noncompliance
- Research-Related Concerns
- Suspension or Termination of Research

Current IRB Event Report Application

- Adverse Device Effect
  - Report only if unanticipated
- Adverse Event or Injury
  - Report only if serious, unexpected, **and** related
- Breach of Confidentiality
  - Report only if involving risk
- Data and Safety Monitoring Board (DSMB) Report
  - Report information altering the risk/benefit profile
- Event Requiring Prompt Reporting
  - Report only when required by the study or sponsor
- Investigator's Brochure Update
  - Report revision(s) to safety information that could alter the risk/benefit profile to subjects

Current IRB Event Report Application

- New information
  - Report unexpected changes in risks or potential benefits, e.g., literature/scientific report
- Protocol deviation, violation, or unintentional change to protocol or procedures
  - Report only those involving risk or with the potential to recur
- Subject complaint
  - Report complaints indicating unanticipated risks or those that cannot be resolved by the research staff
- Unapproved change made to the research to eliminate an apparent immediate hazard to a subject
- Other problem or finding
  - …that could influence safe conduct of the research (e.g., loss of study data, a subject becomes a prisoner while participating in research, etc.)

Clarifications to Policy

Prompt Reporting:

- Audit findings, inquiry, or written report by a federal agency (e.g., FDA Form 483)
- Suspension by the sponsor, investigator, or institutional entity

Routine Reporting:

- IND safety reports from external sites not involving Ohio State research
- Investigator's brochure updates not involving safety information

Clarifications to Policy

- Noncompliance Review

- Events that occur at external sites that do not involve research conducted at Ohio State are not required to be reported promptly via an event report.
  - Amendment should be submitted through Buck-IRB to change the research
  - Investigators should retain copies of all external reports
  - Any change to the risk/benefit ratio should be explained in summary at the time of continuing review

Reporting Considerations

- Expected vs. Unexpected
- Related vs. Unrelated
- Ohio State IRB Jurisdiction
- Internal Event vs. External Event
- UPIRSO- Unanticipated problem involving risks to subjects or others
- Prompt Reporting vs. Routine Reporting

Event Reporting Definitions

- Adverse Event (AE)
  - Any undesirable and unintended effect occurring as a result of intervention, interaction, or collection of identifiable private information in research.
  - Any untoward physical or psychological occurrence in research temporally associated with the use of a medical treatment or procedure regardless of relatedness.

- Serious Adverse Event (SAE)
  - Death
  - Life Threatening
  - Hospitalization (initial or prolonged)
  - Permanent Disability or Damage
  - Congenital Anomaly/Birth Defect

Event Reporting Definitions

- **Unexpected Adverse Event**

  AE not previously observed or is not consistent in nature, severity, or frequency with existing risk information, such as in the investigator's brochure, research protocol, consent form, or other available information (e.g., IND application)

- **Related**

  Associated or having a timely relationship with; a reasonable possibility exists that an outcome may have been caused or influenced by the event in question (e.g., administration of a study drug), although an alternative cause/influence may also be present. Related events may be **definitely, probably, or possibly** related.

Event Reporting Definitions

- **Ohio State IRB Jurisdiction**
  Research reviewed and approved by the Cancer, Biomedical Sciences, or Behavioral and Social Sciences IRB.

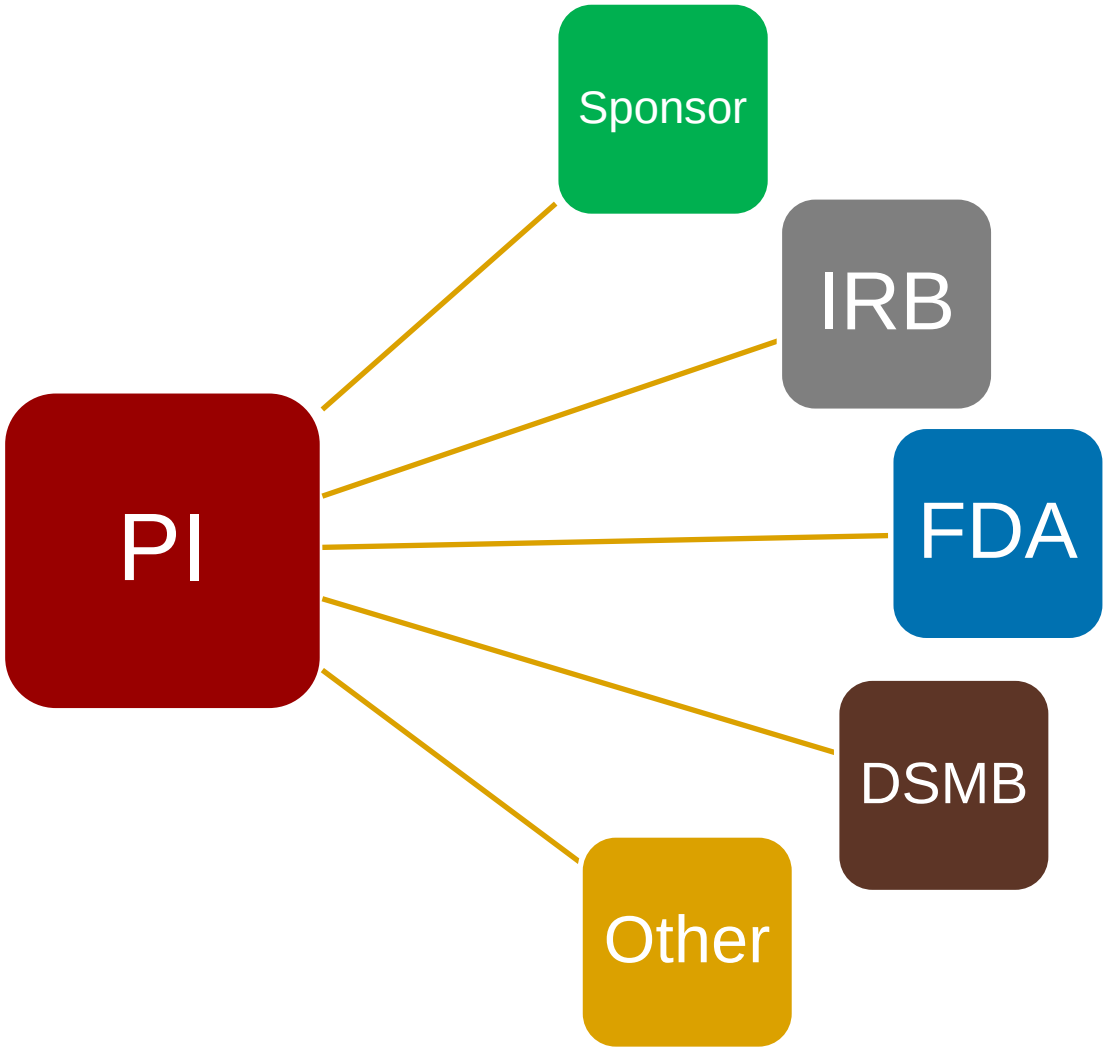
- **Internal Event**
  An event occurring in Ohio State research at a site(s) under an Ohio State IRB's jurisdiction

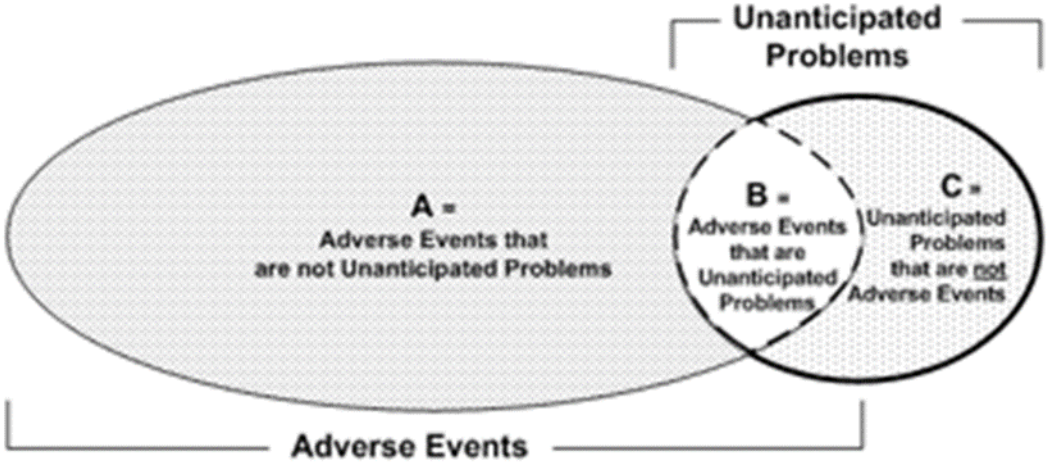
- **External Event**
  An event occurring at a non-Ohio State site over which another IRB has jurisdiction in research that is also occurring at Ohio State.

Event Reporting Definitions

- UPIRSO (Unanticipated Problem Involving Risks to Subjects or Others)
  - Unexpected events that suggest subjects, research staff, or others are placed at greater risk by the research than previously expected.
  - Medical or non-medical in nature
  - Serious, Unexpected, **AND** Related AEs
  - Event may also involve:
    - Subject complaints
    - Protocol deviations

PI Reporting AE & SAE Requirements





Under 45 CFR part 46: Do not report A, Do report (B+C)

Key points:

1. The vast majority of adverse events occurring in human subjects are not unanticipated problems (area A).
2. A small proportion of adverse events are unanticipated problems (area B).
3. Unanticipated problems include other incidents, experiences, and outcomes that are not adverse events (area C).

Assessing Serious Adverse Events for IRB Reporting

1. Is the AE unexpected?
   - Informed Consent Document
   - Protocol
   - Investigator Brochure
   - CAEPR (Comprehensive Adverse Events & Potential Risks list)

2. Is the AE possibly related to participation in research?
   - Temporal relationship to protocol intervention

3. Does the AE suggest that the research places subjects at greater risk of harm than was previously known or recognized for research conducted under Ohio State IRB jurisdiction?
   - Risk listed on the ICF
   - Severity & frequency

Common Corrective Actions
UPIRSO or Noncompliance

- Modification of the protocol and/or consent documents
- Modification of protocol procedures and processes
- Monitoring of the consent process
- Follow-up audits
- PI and/or staff education or mentoring
- Modification of the continuing review cycle
- Additional resources to support investigator's research
- Limitations on investigator's activities (PI privileges)
- Limitation on use of research data
- Study suspension or termination
- Referral to other appropriate university process (e.g., misconduct review).

IRB Incident Notifications

Noncompliance, UPIRSOs, Suspensions, Terminations

Required by Ohio State's Federalwide Assurance

Internal Reporting

- Institutional Official, Dean, Vice Dean for Research, Chair, Co-Investigators
- Other: Director of Sponsored Programs, Technology Commercialization Office, HIPAA Privacy Officer, Legal Affairs, Office of Research Compliance

External Reporting

- Funding Agency, Collaborating Institutions, OHRP, FDA, Participants, Other

Case Studies
IRB Event Reporting

Example 1

AE-

- Participant with acute renal failure at a site under Ohio State IRB jurisdiction
- Probably related to study drug administration
- Resulting in hospitalization
- Renal failure not listed as a known risk in the informed consent

IRB Event Report?

- Yes
  - Serious, Unexpected & Probably Related

UPIRSO?

- Yes
  - Risk not disclosed in the consent form

Prompt Sponsor and FDA Reporting?

- Yes- SAE (hospitalization)

Example 2

AE-

- Participant death at a site under Ohio State IRB jurisdiction
- Probably related to disease progression

IRB Event Report?

- No
  - Serious but Not Related to Research Intervention or Interaction

Prompt Sponsor?

- Yes- Death

Example 3

AE-

- Participant with suicidal ideation at a site not under Ohio State IRB jurisdiction but engaged in Ohio State research
- Resulting in hospitalization
- Unexpected and related to protocol behavioral intervention
- Not listed as a known risk in the informed consent.

IRB Event Report?

- Yes
  - Serious, Unexpected & Related

Prompt Sponsor and FDA Reporting?

- Yes- SAE (hospitalization)

Example 4

AE- IND Safety Report

- Participant with suicidal ideation at a site not under Ohio State IRB jurisdiction and enrolled in research that is not conducted at Ohio State
- Resulting in hospitalization
- Unexpected and related to protocol behavioral intervention
- Not listed as a known risk in the informed consent.

IRB Event Report?

- Depends
  - If implementing changes to eliminate an apparent immediate hazard to participants prior to approval of the amendment= YES

PI Request to Change Research?

- Yes- Buck-IRB Amendment to Research

Example 4 (Cont.)

In the opinion of the PI if the event does not warrant a change in the research or adversely affect Ohio State research

- No Event Report or Amendment to the Research
- A DSMC report or investigator summary reflecting changes to the risk benefit ratio should be provided at continuing review.
- Individual reports should be maintained by the Investigator and not submitted with the continuing review application.

Example 5

Internal Protocol Deviation-

- Incorrect study drug dose provided to subject

Event Report?

- Yes
  - Protocol deviation from the currently approved treatment plan

UPIRSO?

- Yes
  - Incorrect dose may increase risk

Noncompliance?

- Yes
  - Change in study procedures without prior approval

Corrective Action?

- Provide corrective action to avoid dosing errors (SOPs, education, training, etc…), notify subject of error

Example 6

Internal Protocol Deviations-

- Failure to obtain informed consent prior to research activities
- Individuals accessing identifiable information without IRB approval
- Failure to obtain HIPAA authorization

Event Report?

- Yes

UPIRSO?

- Maybe

Noncompliance?

- Yes

Example 7

Updated Sponsor Investigator's Brochure-

- Administrative changes
- Updated the number of clinical trial subjects
- Current study status: actively recruiting subjects

IRB Event Report?

- No
  - No change in risks to subjects

IRB Amendment?

- No

Example 8

Disclosure of Personally Identifiable Information (PII)-

- Study survey collected personal lifestyle risk information
- Correlated survey responses with medical records information
- Inadvertently emailed spreadsheet w/ subject identifiers and data to someone not involved in the study
- Reported the event to the privacy officer

IRB Event Report?

- Yes
  - Unapproved disclosure of PII

UPIRSO?

- Yes
  - Increased risks to subjects

Noncompliance?

- Yes
  - Failure to ensure confidentiality of PII

Case Examples

Contact ORRP With Questions: (614) 688-8457			
Event	**Examples (not all-inclusive)**	**Reporting Criteria**	**How to Report**
Adverse Event (AE)	◦ Participant with acute renal failure at a site **under Ohio State IRB jurisdiction**, probably related to study drug administration, resulting in hospitalization, renal failure not listed as a known risk in the informed consent document or investigator's brochure. ◦ Participant with suicidal ideation at a site **not under Ohio State IRB jurisdiction but engaged in Ohio State research,** resulting in hospitalization, unexpected, related to protocol behavioral intervention, not listed as a known risk in the informed consent.	**An adverse event that is:** ✓ Serious, ✓ Unanticipated, **and** ✓ Related	**Buck IRB Event Report within 10 Business Days**
AE Reports **(PI Request to Change Research Due to New or Increased Risk)**	Participant experienced event at a site **not under Ohio State IRB jurisdiction and enrolled in research that is <u>not</u> conducted at Ohio State** ◦ IND Safety Reports ◦ MedWatch Reports ◦ CIOMS Reports	**In the opinion of the PI an unanticipated problem that adversely affects the:** ✓ risk/benefit ratio of the study, or ✓ rights, safety, or welfare of the participants or others, or ✓ integrity of the study	**Buck IRB Amendment to Research Request** *If implementing changes to eliminate an apparent immediate hazard to participants prior to approval of the amendment, please also submit a Buck IRB Event Report within 10 Business Days.*

Next Steps

- Education & Outreach
  - IRBs & Research Staff
- Buck-IRB Applications
  - Event Report
  - Continuing Review
- PI Correspondence
  - No Review Required
  - Completeness Verified
  - No Further Action
- Additional FAQs/Guidance for Researchers

Questions?


OSU.EDU
Help BuckeyeLink Map Find People Webmail Search Ohio State
OFFICE OF RESEARCH
Office of Responsible Research Practices
THE OHIO STATE UNIVERSITY
Home About Us Animal Care and Use Biosafety Human Subjects Resources Contact Us News
Protecting Human Subjects in Research at Ohio State
Human Subjects
The Human Research Protection Program is responsible for all Ohio State research involving human subjects. The HRPP's primary responsibility is to protect the rights and welfare of human research subjects, in accordance with Department of Health and Human Services (DHHS) and Food and Drug Administration (FDA) regulations.
NEWS
Spring 2015 IRB Newsletter now available
POSTED: MARCH 26, 2015
New System for IRB and Exempt Submissions