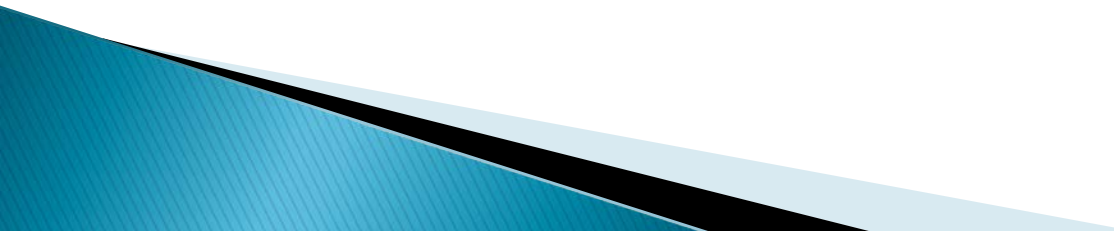


# Reportable Events

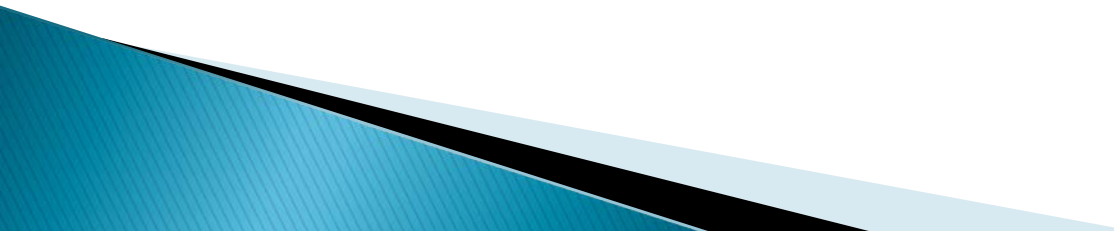


# Types of Reportable Events

- ▶ Unanticipated Problems Involving Risk to Subjects or Others
    - Adverse Events that are UAPs
    - Other Unanticipated Problems Involving Risk to Subjects or Others
  - ▶ Deviations or Noncompliance
- 

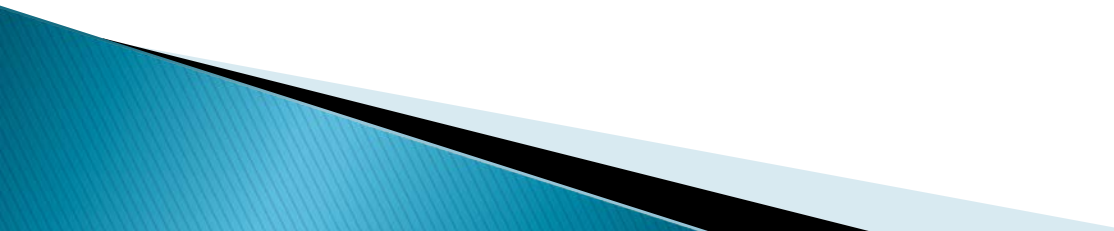
# Unanticipated Problem Definition

Any accident, experience, or outcome that:

- Is unexpected in nature, severity or frequency
  - Is related or possibly related to a subject's participation in the research
  - Places subjects or others at a greater risk of harm (physical, psychological, economic, or social harm) than was previously known or recognized
- 

# Adverse Event Definition

Any unfavorable medical occurrence in human subjects, including abnormal signs (e.g., abnormal physical exam or laboratory findings), symptoms, or disease temporally associated with, but not necessarily considered related to, the subject's participation in the research.

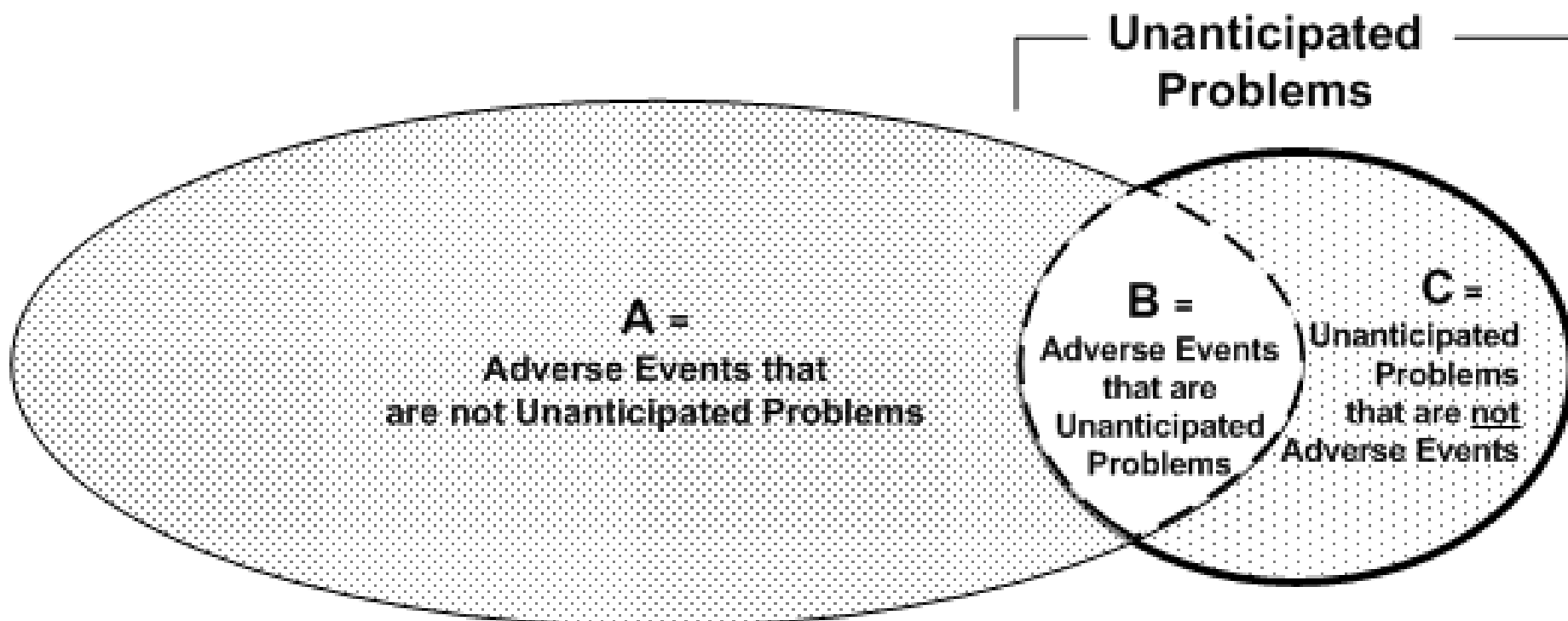


# “Other” Unanticipated Problem

Unanticipated problems involving risk to human subjects or others that are **NOT** adverse events

(Everything else)

# OHRP's Venn Diagram



**Under 45 CFR part 46: Do not report A; Report B and C.**

# FDA Guidance (January 2009)

AE should be considered an unanticipated problem involving risk to human subjects and reported to the IRB, only if:

- **Unexpected**, and
- **Serious**, and
- would have **implications for the conduct of the study** (significant, and usually safety-related change in the protocol like revising inclusion/exclusion criteria, new monitoring requirements, ICF or IB)

<http://www.fda.gov/cder/guidance/OC2008150fnl.pdf>

# Unexpected adverse event

Not identified by nature, severity or frequency in the investigator's brochure, sponsor protocol or current University IRB-approved research protocol or informed consent document, taking into account the characteristics of the subject population being studied



# DEFINITIONS:

## Serious Adverse Event

- fatal or life-threatening
- requires or prolongs inpatient hospitalization
- produces a persistent or significant disability/incapacity
- results in a congenital anomaly/birth defect
- based on appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed above

# DEFINITIONS:

## Related to the Research

- ▶ **Possibly related** – In the opinion of the principal investigator, there is a **reasonable possibility** that the incident, experience, or outcome may have been caused by the procedures involved in the research
- ▶ **Related** – In the opinion of the principal investigator, the incident, experience or outcome **more likely than not** was caused by the procedures involved in the research

# Reporting Requirements

**Internal adverse events** meeting all 3 of the following must be reported:

- (i) Unexpected;
- (ii) Serious; and
- (iii) Related or Possibly Related to the research intervention

# Reporting External Adverse Events

**External adverse events** meeting all 3 of the following must be reported:

- (i) Unexpected;
- (ii) Serious AND suggests that the research places subjects or others at greater risk than was previously recognized; and
- (iii) Related to the Research Intervention

# Examples of “Other” UAPs

- ▶ Any accidental or unintentional deviation from the IRB–approved protocol that involved risks or has the potential to recur;
- ▶ Any deviation from the protocol taken without prior IRB review to eliminate apparent immediate hazard to a given research subject;
- ▶ Any publication in the literature, safety monitoring report, interim result, or other finding that indicates an unexpected increase in the risk to benefit ratio of the research;

## Examples of “Other” UAPs (cont.)

- ▶ Any complaint of a subject that indicates an unanticipated risk or which cannot be resolved by the research staff;
- ▶ Any other untoward event that affects the welfare or the privacy, confidentiality or other rights of research subjects or members of their family;
- ▶ Any other untoward event that presents a risk to investigators and research staff involved in the conduct of the research;
- ▶ Over-enrollment

# Deviation or Non-Compliance

Failure on the part of the investigator or any member of the study team to follow the terms of University of Pittsburgh IRB approved protocol or to abide by applicable laws or regulations, or University of Pittsburgh IRB policies (includes protocol deviations).

# What Happens at the IRB?

Adverse Events are reviewed by IRB Adverse Event Coordinator (AERRC)

- Request additional information if needed
- Dr. Guido, IRB Chair, notified if immediate action for subject safety may be required
- Assign to next convened meeting with appropriate expertise
- Assigned primary and secondary reviewer



# What happens at the IRB?

- ▶ “Other UAPs” and “Deviations” are first reviewed by the IRB Chair and the Adverse Event Coordinator
- ▶ An initial determination is made regarding:
  - Additional information required
  - Refer to an IRB Committee with appropriate expertise (for UAPs)
  - Compliance related issues typically are assigned to Committee F
  - No further action is required

# What happens at the IRB?

- ▶ UAPs and Deviations must be reviewed by an IRB Committee if:
  - May represent serious non-compliance
  - May represent continuing non-compliance
  - May meet the determination of an unanticipated problem involving risk to subjects or others

# IRB Convened Meeting Process

## Committee actions

- Request more information, request modifications, suspend study, interventions, and/or enrollment, or determine that no further action is needed
- Decision on whether subjects must be notified of event
  - Require modification to revise consent form
  - Require modification to submit a consent form addendum

# Required Modification of the Associated Protocol

- ▶ Instruct the investigator to develop an addendum consent form to provide information concerning the event to subjects currently enrolled in the study.
- ▶ Require the investigator to perform additional follow-up or monitoring of the enrolled subjects
- ▶ Revise the timeframe for continuing University IRB review

# Possible Committee Determinations

**Represents Serious Non-Compliance**, defined as:

Non-compliance that, in the judgment of the University IRB, significantly adversely affects the rights or welfare of participants, or significantly compromises the quality of the research data.

Examples of non-compliance that are considered to meet the definition of serious non-compliance include, but are not limited to:

- ▶ performing non-exempt human subject research without obtaining University IRB approval
- ▶ implementing substantial modifications to a research study without obtaining formal University IRB approval
- ▶ failing to systematically obtain research subjects' informed consent as required by the IRB approved protocol
- ▶ failing to comply with federal regulations governing human subject protections (this includes activities of the University IRB and/or University IRB Office staff)

# Possible Committee Determinations

**Represents Continuing Non-Compliance**, defined as:

Non-compliance that has been previously reported or a pattern of ongoing non-compliance that, in the judgment of the University IRB, significantly adversely affects the rights and welfare of participants or significantly compromises the quality of the research data.

# Possible Committee Determinations

- ▶ **Represents an Unanticipated Problem Involving Risk to Human Subjects or Others:**  
Any accident, experience, or outcome that meets all of the following criteria:
  - unexpected in terms of nature, severity, or frequency;
  - related, or possibly related, to a subject's participation in 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.

# Correspondence

- ▶ Letter to PI:
- ▶ Letter to OHRP
- ▶ Letter to FDA
- ▶ Letter to Funding Agency
- ▶ Letter to Institutional Official



# Questions?

Specialized education  
available upon request:

[askirb@pitt.edu](mailto:askirb@pitt.edu)