

Problems or Events that Require Prompt Reporting to the IRB

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Think of What Occurs During the Life of Your Research Study

You have an idea:

- design a research study that will involve humans as participants
- obtain IRB approval for the research
- conduct the study
- analyze your data
- report your results

Think of What Can Go Wrong During the Study

- An adverse event
- What else?
 - ?
 - ?
 - ?
 - ?
 - ?

Think of What Can Go Wrong During the Study (cont.)

- Were all of these problems or events expected?
- Might one or more have been unexpected?
- Might one or more involve a new risk?

What Do Federal Regulations Require When a Problem Occurs?

Federal regulations require prompt reporting to the Institutional Review Board (IRB), appropriate institutional officials, sponsor, coordinating center and the appropriate regulatory agency head of unanticipated problems involving risks to subjects or others that occur in the course of a subject's participation in a research study. (45 CFR 46.103(b)(5)(i) and 21 CFR 56.108(b)(1)).

Definition

Unanticipated

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.

Definition - Unanticipated Problem Involving Risks to Subjects or Others

Any problem or event that the investigator or staff person considers to:

- Be unanticipated, and
- Indicate 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.

Definition

Possibly Related

There is a reasonable possibility that the incident, experience, or outcome may have been related to the research. The DUHS IRB interprets "reasonable possibility" to mean "more likely than not". Therefore "possibly related" means "more likely related than unrelated".

"The problem or event was more likely related to the research than unrelated to it."

What Must be Promptly Reported to the IRB?

Any problem or event that the investigator or staff person considers to:

- Be unanticipated, and
- Indicate 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.

Think "A new risk".

Think of what may happen that is unanticipated/unexpected

- An interim analysis or safety monitoring report indicates that the frequency or magnitude of harms or benefits might be different from those initially presented to the IRB.
- A paper is published from another study that shows that the risks or potential benefits of the research might be different from those initially presented to the IRB.

Think of what may happen that is unanticipated/unexpected (cont.)

- An allegation of non-compliance with protocol requirements (including protocol deviations or violations) or IRB policies.
- A breach of privacy or confidentiality.
- A change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
- Incarceration of a subject in a protocol not approved to enroll prisoners.

Think of what may happen that is unanticipated/unexpected (cont.)

- A subject's complaint when it indicates unexpected risks, or it cannot be resolved by the research team.
- A protocol violation (meaning an accidental or unintentional change to the IRB approved protocol) that harmed subjects or others or that indicates subjects or others might be at increased risk of harm.
- An unanticipated adverse device effect.

Think of what may happen that is unanticipated/unexpected (cont.)

- An event that, as dictated by the protocol, requires urgent reporting to the sponsor.
- Any change made to the research without prior IRB approval in order to eliminate apparent immediate harm.
- A sponsor imposed suspension for risk.
- Any other problem that the investigator considers to be unanticipated and indicates that subjects or others are at increased risk of harm (Think: "A new risk".)

What Must be Reported to the IRB?

- An expected adverse event?
- An unanticipated adverse event?
- The loss of a subject's signed consent document?
- A set of safety laboratory tests that cannot be performed because the samples were destroyed in transit to the lab?
- The injury of a study coordinator while driving to interview a research subject?
- An unexpected excess of expected adverse events?

**All must be reported
to the IRB.**

**But not all must be
reported promptly.**

Prompt Reporting Requirements

Report within 24 hours of learning about:

- Any subject's death that was unanticipated and was more likely related to the research than unrelated.
- Report initially by email or fax to the IRB.
- Follow the initial report within 5 business days by submitting a *Notification of a Problem or Event Requiring Prompt Reporting to the IRB* ("Prompt Reporting Form" available on the IRB web site or under Forms in the e-IRB system).

Prompt Reporting Requirements

(cont.)

Report within 5 business days of learning about:

- Any serious adverse event (as defined by the protocol) that was unanticipated and was more likely related to the research than unrelated.
- Submit a *Notification of a Problem or Event Requiring Prompt Reporting to the IRB* ("Prompt Reporting Form" available on the IRB web site or under Forms in the e-IRB system).

Prompt Reporting Requirements (cont.)

Report within 10 business days of learning about:

- Any other unanticipated problem or event that was more likely related to the research than unrelated (Think *"A New Risk"*).
- Submit a *Notification of a Problem or Event Requiring Prompt Reporting to the IRB* ("Prompt Reporting Form" available on the IRB web site or under Forms in the e-IRB system).

What Must be Reported Promptly to the IRB?

- An expected adverse event?
- An unanticipated adverse event?
- The loss of a subject's signed consent document?
- A set of safety laboratory tests that cannot be performed because the samples were destroyed in transit to the lab?
- The injury of a study coordinator while driving to interview a research subject?
- An excess of expected adverse events?

Reporting at Continuing Review

You will be prompted to:

- Summarize events requiring Prompt Reporting.
- If no events occurred that required prompt reporting, you will be asked if there has been an unexpected excess of expected adverse events.
- If you answer "No", you will be asked to confirm that "Adverse events occurred at the expected frequency and level of severity as documented in the research protocol, any associated research documents, and the informed consent document."

Reviewing the Continuing Review Application

The Primary Reviewer of a study undergoing Continuing Review will be asked:

Were any events described that required prompt reporting to the IRB?

- If yes, please explain the effect of those events on the current risk/benefit assessment.
- If no, has an unexpected excess of an expected adverse event occurred? If yes, has this been promptly reported to the IRB? If no, include this as a required modification to secure approval of the continuing review submission.

Please contact your IRB Specialist if you have questions about this or any IRB policy or procedure.

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One closing question

Is the expiration date of an IRB-approved protocol:

- The last date the protocol is approved?
- The first date the protocol is not approved?