



Prompt Reporting for Investigators and Research Staff Conducting Research, IRB's 1, 2, and 3

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Case Study: An Introduction

- For this introductory case study, assume that the principal investigator, “The Professor,” is conducting research that involves a psychological evaluation of individuals who have indicated a familial occurrence of alcoholism.
- Now “The Professor” discovers during a weekly research staff meeting that a coordinator, Gilligan, who has not been approved by the IRB to conduct the research, has obtained informed consent from 4 individuals.
- Introductory Question 1: Is The Professor required to promptly report this event to the IRB?
 - A. Yes
 - B. No

Case Study: An Introduction

Now “The Professor’s” study has a genetic sub-study component with a separate informed consent document.

- While conducting the research, “The Professor” realizes he has mistakenly kept the blood vials in his private (non-UIC) office without IRB permission.
- Neither the protocol nor the informed consent list this alternative tissue banking location.

Case Study: An Introduction

- Introductory Question 2: Why would this be an event that needs to be promptly reported?
 - a. The event represents a change to the protocol made without IRB approval.
 - b. The event does not need to be reported if the Professor returns the vials to the UIC research site immediately and does not tell anyone.

Case Study: An Introduction

- Now a research coordinator, Ginger, takes folders containing participant name, contact information, and genetic test results (identifiable information), home to analyze the data.
- On her way home, she leaves the folders of information in her grocery cart. Someone finds the folder and calls "The Professor."
- Introductory Question 3: Which of the following is a reason this event must be promptly reported to the IRB?
 - a. Ginger had intent to take participant information away from the research setting
 - b. The participant information was identifiable
 - c. Both a and b
 - d. Neither a nor b

Case Study: An Introduction

- Assume that Mrs. Howell, a research coordinator, receives a telephone call from a participant in the study.
- The participant complains that they were improperly billed for items and services that the informed consent promised for free.
- Introductory Question 4: Is this an event that requires prompt reporting to the IRB?
 - A. Yes
 - B. No

Training Goals

- The prompt reporting policy and procedure to meet the following three goals:
 1. To increase the reporting and capturing of internal adverse events determined by the investigator to be unanticipated and related to the research.
 2. To enforce a restrictive reporting of external adverse events so that the IRB can concentrate on the most important events.
 3. To capture other events that affect patient safety and non-compliance.



Desired Outcome

- In this way, the IRB can have a defined focus and be aware of and act on the most relevant and important problems and events.

Essential Definitions (1 of 4)

1. **Unanticipated Problem:** means that the specificity, severity or frequency of the event is not expected based on (a) information contained in the protocol, investigator's brochure, informed consent document, drug or device product information or other research materials; and (b) the characteristics of the subjects, including underlying diseases, behaviors, or traits.
2. **Related or possibly related to the research:** means the event is more likely than not to have been caused by the procedures associated with the research.

Essential Definitions (2 of 4)

3. **Serious Adverse Event:** Adverse events classified as serious include those resulting in death, life-threatening injury, hospitalization or prolongation of hospitalization, persistent or significant disability, or a congenital anomaly or birth defect.
 - Events not meeting the above criteria but requiring intervention to prevent one of these outcomes are also considered serious adverse events.

Essential Definitions (3 of 4)

4. Protocol Violation: Any accidental, unintentional or intentional deviation or variance in the conduct of the research that is implemented prior to IRB approval. Protocol violations that cause harm to subjects or others, place them at increased risk of harm, impact the scientific integrity, have the potential to recur or represent possible serious or continuing non-compliance require prompt reporting.
 - o Protocol violations not meeting at least one of the criteria in the preceding sentence do not require reporting to the IRB. They should be reported to the sponsor as described in the protocol and written documentation of their occurrence filed with the investigator's study records.

Essential Definitions (4 of 4)

5. Internal: Events occurring at UIC, JBVAMC or other sites where the UIC IRB has oversight responsibility for the research (e.g., UIC is the principal site or coordinating center for a multi-center trial, UIC IRB is IRB of record).
6. External: Events occurring at non-UIC sites where UIC IRB has no oversight responsibilities.

Examples of Problems or Events that Require Prompt Reporting

- Adverse Events or Adverse Effects:
 - Internal adverse events determined by the investigator to be unanticipated and related to the research
 - External adverse events determined by the investigator, sponsor, coordinating center or DSMB/DMC to represent an unanticipated problem (i.e., unanticipated, related, and increased risk of harm)
 - Changes to the protocol made without IRB approval to eliminate apparent immediate harm to subjects
 - Unanticipated adverse device effects

Examples of Problems or Events that Require Prompt Reporting

- Non-Compliance
 - Breach in confidentiality
 - Incarceration of a subject in a protocol not approved to enroll prisoners
 - Protocol violations that cause harm to subjects or others, place them at increased risk of harm, impact the scientific integrity, have the potential to recur or represent possible serious or continuing noncompliance.
 - Observed or apparent non-compliance

Examples of Problems or Events that Require Prompt Reporting

- Other Unanticipated Events/Problems
 - Publication, interim analysis, safety monitoring report, or undated investigator's brochure that indicates an unexpected change to the risks or benefits of the research
 - Change in FDA labeling or withdrawal from marketing of a drug, biologic or device used in the research
 - Subject complaints that indicate an unanticipated problem or event which cannot be resolved by the research staff
 - Administrative hold by investigator or sponsor
 - Events requiring prompt reporting by the protocol or sponsor.

What is the time line for reporting?

- Reporting is required within five working days of becoming aware of the event for:
 1. Internal adverse events considered serious as defined in previous slides (e.g., death, life threatening injury);

and
 2. Changes to the protocol made without IRB approval to eliminate apparent immediate harm to subjects.

What is the time line for reporting?

- Report **within 10 working days** of discovering or being notified of the event is required for other incidents.
- PIs also responsible for reporting adverse events and problems to the sponsor and any other agencies as specified in the protocol, data safety monitoring plan or other agreements.

What form should be used?

- *Prompt Reporting to the IRB* form
 - Available on the UIC OPRS website (see next slide)
 - Link:
<http://tigger.uic.edu/depts/ovcr/research/protocolreview/irb/forms/0257.doc>

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FORM - Prompt Reporting to the IRB

Version: 2.0
Date: 07/22/2008

Office for the Protection of Research Subjects (OPRS) Institutional Review Board

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Chicago, IL 60612-7227
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www.research.uic.edu/protocolreview/irb

This form should be used to report:

- unanticipated problems involving risks to subjects or others,
- new information that unexpectedly alters risks or benefits,
- significant protocol violations,
- administrative hold by the investigator or sponsor,
- findings or allegations of noncompliance, and
- other events that require prompt reporting according to UIC policy (see complete list in Section III below).

Definitions

Unanticipated problems involving risks to subjects or others (i.e., unanticipated problem) refers to a problem, event or information item that is not expected, given the nature of the research procedures and the subject population being studied; and suggests that the research places subjects or others at a greater risk of harm or discomfort related to the research than was previously known or recognized.

Unanticipated means that the specificity, severity or frequency of the event is not expected based on (a) information contained in the protocol, investigator's brochure, informed consent document, drug or device product information or other research materials; and (b) the characteristics of the subjects, including natural progression of any underlying diseases.

Related means that the event is more likely than not to have been caused by the procedures associated with the research.

Greater risk of harm means the research causes harm (including physical, psychological, economic,

What happens once the investigator submits the form? (1 of 2)

- A senior OPRS staff member:
 - Reviews the prompt reporting form submission for a factual basis and
 - enters the report in a tracking log that is used to detect patterns.
- If a factual basis does not exist:
 - Staff member documents that the matter is closed on a review guide and
 - communicates this finding to the investigator.

What happens once the investigator submits the form? (2 of 2)

- If a factual basis exists:
 - Senior OPRS staff member makes a compliance determination and
 - may recommend the event to the IRB Chair, who reviews the matter.
 - The matter is then also brought to the convened IRB.
- OPRS will work in an efficient manner to resolve the matter and communicate the finding to the investigator.
- Please note that investigations may need to take place, the resolution of which may take some time.

Case Study

- Thurston Howell III, a co-investigator, identifies that a participant has self-inflicted a life threatening injury and immediately adds an additional off-protocol session without IRB approval to evaluate whether the participant is at risk for suicide to eliminate immediate harm.
- The additional session focusing on the suicidal risk evaluation is not included in the protocol or within the informed consent form.

Case Study

Case Study Question 1: Would the additional off-protocol session need to be promptly reported to the IRB?

- a. No, the session is not a drug intervention and therefore does not need to be reported
- b. Yes, the session is a change to the protocol that has been made without IRB approval to eliminate immediate harm to subjects
- c. No, the session already happened without IRB approval to eliminate immediate harm, and IRB approval cannot be retroactive, so no reporting is necessary
- d. No, the session is minimal risk and only greater than minimal risk events need to be reported to the IRB

Case Study

- Now the principal investigator, “The Professor,” determines that the additional session conducted by Hurston Howell III focusing on suicidal risk evaluation must be promptly reported to the IRB as the session is a change to the protocol that has been made without IRB approval to eliminate immediate harm to subjects

Case Study Question 2: What is the time frame for reporting?

- a. When the next continuing review application is submitted
- b. Within 10 working days of becoming aware of the event
- c. Within 5 working days of becoming aware of the event
- d. When the next amendment is submitted for review

Case Study

- Now the main psychological study is a multi-center trial where “The Professor’s” institution has no oversight.
- Assume a site that is part of the multi-center consortium reports that a participant has died from liver disease. Assume a data safety monitoring board determines that this event is unanticipated and not related to the research.

Case Study Question 3: Since UIC is not the main site, does the death need to be reported to the IRB?

- a. Yes
- b. No

Case Study

- The principal investigator, “The Professor,” did not include prisoners as a subject population on his IRB application. A properly consented participant in the main study is placed on house arrest while a participant in the study.

Case Study Question 4: Does this event, which is unanticipated and related to the research, need to be promptly reported to the IRB?

- a. Yes, because the IRB has not approved the enrollment of prisoners in the research.
- b. No, because the participant is not a prisoner because he was placed on house arrest after being enrolled in the research.

(Side bar- Does “unanticipated and/or related” matter in this scenario?)

Case Study

- Now a participant in the main psychological study has been hospitalized for a psychiatric condition determined to be related to the main study sessions. Assume that this event is both unanticipated and the hospitalization represents a change to the protocol that the IRB has not approved.

Case Study Question 5: What is the timeframe for reporting this event to the IRB?

- a. When the investigator implements a corrective action plan
- b. Within 5 working days of becoming aware of the event
- c. Reporting can wait until the participant demonstrates that he or she cannot re-enter the research study
- d. With the next amendment form submission

Case Study

- Now assume that a genetic sub-study exists with a separate consent form. Assume for purposes of this question only that a research coordinator, Mrs. Howell, is a registered nurse and properly credentialed. She is responsible for obtaining blood samples from sub-study participants.
- Assume that she uses the same needle when she collects the blood samples. Some subjects appear to be infected with hepatitis after this event. The Professor determines that this is related to the research.

Case Study Question 6: Is this an event that would need to be promptly reported to the IRB?

- a. Yes
- b. No

Case Study

- Now the principal investigator, “The Professor,” determines the subjects’ hepatitis exposure may be life threatening.

Case Study Question 7: What is the appropriate time frame for reporting this event?

- a. Within the time frame described for reporting to the sponsor in the clinical trial agreement
- b. Within the infectious disease reporting time frame provided by the Centers for Disease Control
- c. Within 5 working days of becoming aware of the event
- d. Within the infectious disease reporting time frame as required by Illinois state law

Review: The Time Line for Reporting

- Reporting is required within five working days of becoming aware of the event for:
 1. Internal adverse events considered serious as per slides (e.g., death, life threatening injury);

and
 2. Changes to the protocol made without IRB approval to eliminate apparent immediate harm to subjects.

Review: The Time Line for Reporting.

- Reporting **within 10 working days** of discovering or being notified of the event is required for other incidents.
- The investigator is also responsible for reporting adverse events and problems to the sponsor and any other agencies as specified in the protocol, data safety monitoring plan or other agreements.

Policy and Link:

- Policy: Unanticipated Problems and Other Events Requiring Prompt Reporting
- Link:
<http://tigger.uic.edu/depts/ovcr/research/protocolreview/irb/policies/0279.pdf>



Questions and Answers

- Questions?
- Comments?