
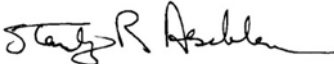


Appalachian State University Research Protections and Institutional Review Board Standard Operating Procedures		
SOP #8 Revision #	TITLE: Unanticipated Problems Involving Risks to Subjects or Others, Adverse Events, and Other Problems	Date Effective: 1/7/2013 Revision Date:
Approved By: RP Director	Signature 	Date
Approved By: IRB Chair	Signature 	Date

PURPOSE

Federal regulations require the University to establish written procedures for ensuring prompt reporting of any unanticipated problems involving risks to subjects or others to the IRB, appropriate institutional officials, any supporting department or agency head.

GENERAL DESCRIPTION

Researchers must report unanticipated problems involving risks to subjects or others to Research Protections and the IRB for review. The IRB makes the final determination of whether an event is an unanticipated problem involving risks to subjects or others.

Definitions

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.

Unrelated: Unassociated or without a timely relationship; evidence exists that an outcome is definitely related to a cause other than the event in question.

Adverse event (AE): Any undesirable and unintended (although not necessarily unexpected) effect occurring as a result of interventions, interactions, or collection of identifiable private information in research.

Unexpected Adverse Event: An adverse event that has not been 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 for an investigational drug).

Serious Adverse Event (SAE): An adverse event that is fatal or life threatening; permanently disabling; requires or prolongs hospitalization; or results in significant disability, congenital anomaly, or birth defect; or an event which based upon appropriate medical judgment may

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jeopardize the subject’s health and require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Unanticipated problems involving risks to subjects or others: Unexpected events (given the nature of the research procedures and subject population) that suggest subjects, research staff, or others are placed at greater risk by the research than was previously known or recognized. Unanticipated problems involving risks to subjects or others may be medical or non-medical in nature, and include, but are not limited to, serious, unexpected, and related adverse events.

RESPONSIBILITY

Execution of SOP: Principal Investigator (PI)/Study Personnel, Research Protections (RP) Staff, IRB Chair, IRB.

PROCEDURES

Event Reporting

1. Investigators and research staff are responsible for promptly reporting unanticipated problems involving risks to subjects or others to the IRB and Research Protections. These reports may include adverse events, subject complaints, protocol deviations, and other untoward events involving risk. Events that require prompt reporting include the following types of events:
 - a. Adverse events or injuries that are serious, unexpected, and related
 - b. Breaches of confidentiality involving risks
 - c. New information indicating an unexpected change in risks or potential benefits (e.g., literature/scientific reports or other published findings)
 - d. Protocol deviations, violations, or other accidental or unintentional changes to the protocol or procedures involving 1) risks to subjects or others; 2) a likelihood of recurrence; or 3) an alteration in the risk/benefit profile
 - e. Subject complaints indicating an unanticipated risk, or complaints that cannot be resolved by the research staff
 - f. Unapproved changes made to the research to eliminate an apparent immediate hazard to a subject
 - g. Data and Safety Monitoring Board (DSMB) reports, interim analyses, or other oversight committee/monitoring reports altering the risk/benefit profile
 - h. Events requiring prompt reporting according to the protocol, sponsor, or funding agency
 - i. Adverse device effects that are unanticipated

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- j. Investigator's brochure or consent form updates/revisions to safety information (excluding routine updates)
 - k. Other problem or finding (e.g., loss of study data or forms, a subject becomes a prisoner while participating in research, etc.) that an investigator or research staff member believes could influence the safe conduct of the research.
2. Investigators and research staff are also responsible for reporting adverse events involving anticipated risks, and serious adverse events that are unrelated to the research. These events do not require prompt reporting. Examples of these types of events include:
- a. Potential risks and adverse events that may be reasonably anticipated (i.e., "expected") and are described in the informed consent process
 - b. Adverse events or injuries that are non-serious, expected, or unrelated
 - c. Deaths not attributed to the research, (e.g., from "natural causes," accidents, or underlying disease) and the investigator has ruled out any connection between the study procedures and the participant's death
 - d. DSMB reports, interim analyses, or other reports, findings, or new information which does not alter the risk/benefit profile
 - e. Investigator's brochure updates not involving safety information
 - f. Protocol deviations or violations unlikely to recur and not involving risks to subjects or others
 - g. Subject complaints that were resolved or complaints not involving risks
 - h. Adverse device effects that are non-serious, anticipated, or unrelated
 - i. Problems or findings not involving risk or the risk/benefit profile unless the investigator or research staff member believes the information could affect participants' willingness to continue in the research.
3. Method and timeframe for reporting of events
- a. Events that require prompt reporting must be reported to Research Protections/IRB using the Event Report Form on the Research Protections website.
 - i. An event which results in the temporary or permanent interruption of study activities to avoid potential harm to subjects must be reported within 48 hours of the investigator becoming aware of the event whenever possible.
 - ii. An event that is a serious adverse event and an unanticipated problem must be reported within 7 days of the investigator becoming aware of the event.
 - iii. All other events requiring prompt reporting must be reported within 10 days of the investigator becoming aware of the event.
 - b. Events that do not require prompt reporting must be reported to the IRB at Continuing Review or study closure, whichever occurs sooner.

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- c. All adverse events must be reported to any monitoring entity (e.g., research sponsor, statistical center, DSMB) if required under the monitoring provisions described in the IRB approved protocol. If the monitoring entity determines the adverse event is an unanticipated problem, the PI must report the event to the IRB using the Event Report Form.
- 4. The Event Report form is designed to collect appropriate identifying information for the research protocol; a detailed description of the adverse event, incident, experience, or outcome; an explanation of the basis for determining that the adverse event, incident, experience or outcome represents an unanticipated problem; and a description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the unanticipated problem. Any proposed modifications must also be submitted in accordance with the IRB Review of Modifications and Addendums SOP.

Review Process

- 1. RP staff review event reports for completeness and determination that the event represents a possible unanticipated problem involving risks to subjects or others.
- 2. Reported events that do not meet the criteria for prompt reporting will be sent to the IRB Chair for confirmation. The IRB Chair or designee will review and determine whether the report will be returned to the PI or reviewed through expedited review.
 - a. If appointed, expedited reviewers will have access to the complete protocol file, including previously reported events, for review. The IRB Chairperson or expedited reviewer will determine if the report raises new concerns about risks and will recommend further review by the convened IRB, as necessary, for a final determination. The IRB Chair or designee may suspend or terminate approval of an investigator’s research if necessary to assure the protection of research participants.
- 3. Reported events determined during screening or expedited IRB review to represent possible unanticipated problems involving risks to subjects or others will be sent to the IRB for full board review. Modifications proposed by the investigator or IRB reviewer that represent more than minor changes will also be reviewed by the convened IRB. The Chair or designee with relevant expertise will serve as the primary reviewer. Copies of the reports, all other information provided by the investigator, and current consent documents (or verbal scripts) with any proposed changes will be provided to all IRB members. Sections from the protocol, previous event reports, and other relevant information or reference materials will also be provided, as applicable. The complete protocol file will be available to any IRB member upon request prior to or during the convened IRB meeting.

IRB Review Outcomes

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1. The IRB will determine by full board review whether the event is an unanticipated problem involving risks to subjects or others and if further action is necessary. Action(s) will be based on the nature of the event, degree to which research participants are placed at risk, occurrence of previous problems, and whether the affected research protocol continues to satisfy the requirements for IRB approval. The IRB will consider the rights and welfare of participants when suspending, terminating, or modifying research. The types of actions that the IRB may consider for any event include, but are not limited to:
 - a. Modification(s) of the research protocol (e.g., procedures, inclusion/exclusion criteria)
 - b. Modification(s) of the consent process or consent form
 - c. Approve continuation of research without changes;
 - d. Providing additional information to current research participants (required when such information may relate to their willingness to continue in the research)
 - e. Providing additional information to past research participants
 - f. Reconfirming consent of current research participants
 - g. Requiring additional follow-up/monitoring for current and/or past research participants
 - h. Monitoring of the research (including audits) or consent process
 - i. Education or mentoring for the principal investigator and/or research staff
 - j. Additional reporting, including modification of the continuing review schedule
 - k. Requiring additional resources to support the investigator’s research activities
 - l. Placing limitations (e.g., restriction to co-investigator status) on the investigator’s research activities or use of research data
 - m. Suspending or terminating the research
 - n. Suspending enrollment of new subjects
 - o. Referral to other appropriate university process (e.g., misconduct review).
2. The IRB’s determination and action(s), including votes taken, will be recorded in the meeting minutes. The requirements for quorum and majority apply.
3. Investigators will be notified in writing by the IRB Chairperson of decisions regarding events determined not to represent unanticipated problems involving risks to subjects or others. Suspended IRB approval may be reinstated, as appropriate, based on the outcome of the full board review.
4. If the IRB determines that an event is an unanticipated problem involving risks to subjects or others, or if the Board suspends or terminates approval of research that is associated with unexpected serious harm to subjects, the investigator(s), IRB, Institutional Official, and the investigator(s)’ Dean and Department Chair (or equivalent) will be notified of the reasons for the IRB’s action in writing by the IRB Chairperson within 14 days of the determination.

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OHRP, FDA (as applicable for FDA-regulated research), the sponsor or any other sponsoring federal Department or Agency, and others (e.g., Office of Sponsored Programs) as necessary, in accordance with Appalachian State University's Federalwide Assurance, will be notified by the IRB Administrator in writing within 30 days. The content of the report will conform to OHRP requirements for incident reporting.

5. Records of reports and reviews of events representing possible unanticipated problems involving risks to subjects or others, including submission materials and communications, are retained by the Office of Research Protections for at least three years, in keeping with federal regulations, applicable state and local laws, and university policies.

SUPPORT PROCESSES AND PROCEDURES

IRB SOPs

REFERENCES

21 CFR 50.25(b)(5), 21 CFR 56.108(b)(1), 21 CFR 812.150(a)(1), 45 CFR 46.103(b)(5)(iii), 45 CFR 46.116(b)(5), OHRP "Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events" (01/15/07), OHRP "Guidance on Reporting Incidents to OHRP" (06/20/11)

Figure 1: Flowchart for Reporting Events to the IRB

