| | University of North Carolina Wilmington<br>Institutional Review Board | Standard Operating Procedure |
|---|---|---|
| | Identifying and Reporting Adverse Events and Unanticipated Problems | #6.7 |

The purpose of this SOP is to outline the steps for identifying and reporting adverse events or unanticipated problems that occur during the course of conducting human subjects research.

## I. General Requirements

The identification, reporting and review of unanticipated problems and adverse events must occur in a timely, meaningful way so that human subjects can be better protected from avoidable harms. Researchers and the IRB should keep in mind that the vast majority of "adverse events" (which are medical in nature) occurring in human subjects research are anticipated problems. In other words, they are known as possible risks of the research. Similarly, often unanticipated problems that are found are not also "adverse events" because they are not medical in nature.

## II. Scope

This SOP pertains to all human subjects research projects that do not qualify for exemption as allowed by 45 CFR 46.101 or as determined by the UNCW IRB.

## III. Applicable Definitions

A. Adverse Event

An untoward or unfavorable medical occurrence in a human subject, including any abnormal sign, symptom, or disease, physical or psychological, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.

B. Unanticipated Problem

Any incident, experience, or outcome that is:

1. Unexpected in terms of its nature, severity or frequency given the research procedures that are described in the protocol-related materials and the characteristics of the subject population being studied, and
2. Is related or possibly related to participation in the research, and
3. Suggests that the research places subjects or others at greater risk of harm (including physical, economic, or social harm) than was previously known or recognized.

## IV. Procedures

A. The principal investigator (PI) of a human subjects research study:

1. Must report serious adverse events that are also unanticipated problems to IRB staff immediately or as soon as possible.
2. Must report adverse events that are not unanticipated problems during continuing review reporting (if applicable).
3. Must report unanticipated problems that are not adverse events in a prompt manner, depending on the seriousness of the problem, and no later than two weeks from the PI becoming aware of the incident.
4. Must provide the IRB with the IRB application number, a detailed description of the incident and outcome, and any corrective actions that were taken in response to the incident.
5. May either contact the IRB office to informally report the incident and obtain guidance, or may submit a New Safety Information form through the IRBIS system to formally report the incident.

B. If contacted for an informal report, IRB staff will help the PI determine if the incident is an adverse event and/or an unanticipated problem, a risk already identified as possible for the research, or some other unrelated problem.
   1. IRB staff may use the Unanticipated Problems and Adverse Events Worksheet (Appendix A) to assist the PI.
   2. If IRB staff believe the incident meets the definition of an adverse event that is also an unanticipated problem, the staff member will instruct the PI to submit the New Safety Information form as a formal report. IRB staff will request review by an IRB co-chair.
   3. If IRB staff believe the incident is an adverse event that is a known risk of the research and adequate information about the risk was provided to subjects during the informed consent process, therefore not an unanticipated problem, IRB staff will instruct the PI to submit a New Safety Information form in IRBIS and subsequently report the incident during the continuing review process (when applicable).

C. When a suspected unanticipated problem is reported regarding a study subject to full board review, IRB staff will place the matter on the next full board meeting agenda, supply the facts of the incident to the committee along with the UP/AE Worksheet (Appendix A) and ask the committee to make a determination on the incident.
   1. If the committee determines that the incident meets all three criteria for an unanticipated problem, the IRB must report the incident within one month of receiving the report from the PI to the Institutional Official and OHRP (if federally funded). Otherwise, no further reporting is required.

D. The IRB may consider the following actions in response to a report of an unanticipated problem or adverse event to eliminate or mitigate newly identified risks:
   1. Change the methods and procedures;
   2. Modify inclusion or exclusion criteria;
   3. Modify or add procedures to monitor subjects;
   4. Suspend enrollment of new subjects;
   5. Suspend research procedures for currently enrolled subjects;
   6. Revise informed consent documents;

7. Provide additional information to previously enrolled subjects, and/or:
8. In extreme cases, suspend or terminate study.

## V. References to Other Applicable SOPs

| SOP Title | SOP # |
|---|---|
| Full Board Review of Research | 5.3 |
| Informed Consent | 6.8 |
| Findings of Non-compliance | 11.1 |

## VI. Responsibilities

| Title | Responsibility |
|---|---|
| IRB Co-chair | Responsible for reviewing reports of adverse events and/or unanticipated problems and making determinations based on UNCW policy, SOPs, and OHRP guidance. |
| IRB Staff | Responsible for providing assistance to PIs in determining whether reporting to the IRB is needed, providing facts to the full board for reports that implicate a study subject to full board review, assisting the IRB in determining further reporting responsibilities. |
| Principal Investigator | Responsible for promptly contacting the IRB when s/he learns of an incident that may be an adverse event and/or unanticipated problem, providing complete and accurate information to the IRB regarding the incident, complying with any requirements identified by the IRB to eliminate or mitigate newly identified risks to subjects. |

## VII. Resources

A. UNCW IRB Website: http://uncw.edu/sparc/integrity/irb.html
B. U.S. Department of Health & Human Services, Office of Human Research Protections, Guidance on Unanticipated Problems Involving Risks and Adverse Events: https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html
C. 45 CFR 46 ("Common Rule"): https://www.ecfr.gov/cgi-bin/text-idx?SID=75addf8360492a28075e3a218631fcdc&pitd=20180719&node=pt45.1.46&rgn=div5
D. Belmont Report: https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html

Appendix A

# Unanticipated Problems and Adverse Events Worksheet

**Is this incident an unanticipated problem?**

1. Was it 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;

   ☐ Yes – unexpected
   ☐ No - expected

2. Is it related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

   ☐ Yes – related to participation in research
   ☐ No – unrelated to participation in research

3. Does it suggest 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?

   ☐ Yes – suggests subjects are at greater risk
   ☐ No – does not suggest subjects are at greater risk

*If all three responses are "Yes," the incident is an unanticipated problem.*

**Is this incident an adverse event?**

1. Was there an untoward or unfavorable medical occurrence (physical or psychological) in a human subject including any abnormal sign, symptom, or disease?

   ☐ Yes – there was an unfavorable medical occurrence

   1a. If yes, was this occurrence *temporally associated* with the subjects participation in the research, *whether or not considered related* to the subjects participation in the research?

   ☐ Yes – temporally associated
   ☐ No – not temporally associated

   ☐ No – there was no unfavorable medical occurrence

*If responses to 1 and 1a are "Yes," the incident is an adverse event.*