

SOP 11.01 - Problems and Adverse Events, Record and Report

1. Objective

This SOP is intended to describe the mechanism for classifying problems that occur during the course of research as well as when and how to record and/ or report such problems to the IRB

2. General Description

Problems occur during research. Having a uniform system for classifying, recording and reporting problems will help protect the safety of human subjects and others, as well as the overall integrity of the study.

Definitions

Problem –encompasses everything that goes wrong during the course of research, though the primary concern is focused around problems as they concern the safety, rights, and welfare of the research participants and others, and/or the integrity of the study.

Adverse Event (AE) – as the term is used in guidance, literature, and common vernacular, is a more specific type of "problem" that is generally considered to be related to the health of a study participant. For the purposes of this SOP, the term "problem" encompasses the more narrowly defined term "adverse event."

Unanticipated problem (UP) – any incident, experience, or outcome that meets all of the following:

1. 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;
2. related or possibly related to participation in the research (in this guidance document, 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
3. suggests 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.

3. Roles & Responsibilities

Execution of SOP: Principal Investigator (PI)/Study Personnel (SP), Office of Research Integrity – Research Protections (ORI-RP) Staff, IRB Chairs / Co-Chairs, IRB Members

It is the primary responsibility of the Principal Investigator and research team members to address and record any problems that occur during the course of research. For the research team member who encounters a study problem, it is recommended that they report the problem to the PI in a timely or immediate manner.

*Immediate action, including one-time changes to approved study procedures, may be taken to avoid apparent and immediate harm, to subjects or others.

Using the basic classification system described in the procedures section below provides a good indication when (not if) a problem needs to be reported to the IRB. All problems need to be reported to the IRB, though, not all problems require immediate reporting or follow-up action. There may be additional requirements or desire to report certain problem events and/ or any follow- up actions to federal agencies or other outside entities.

It is the responsibility of the IRB to assess the problems reported by researchers. Problems that adversely affect the rights and/or welfare of subjects, and/or the integrity of the study may warrant further action (discussed in more

detail below). There may be additional requirements or desire to report certain problem events and/or any follow-up actions to federal agencies, or other outside entities.

4. Procedures

It is highly recommended that the PI utilize the following classification system when recording and assessing problem events. The ORI-RP and IRB will utilize the following classification system when assessing problems reported by the PI or other researchers.

1) Assessment

Rate the problem on the following three scaled criteria:

Not Serious > Serious

Seriousness as being most closely associated with the safety, rights and/ or welfare of study subjects or others.

Anticipated > Unanticipated

The anticipated nature of the event as being most closely associated with potential problem events previously outlined in the study protocol as an expected occurrence, for which there is likely a procedural measure to help any reduce risk of harm. If the problem event is not previously discussed as expected in the study protocol, then it may be classified as unanticipated.

Not Study Related > Study Related

The relatedness of the event as being most closely associated, with participation in the study, or having been affected by the presence of the study.

2) Reporting

If the problem event is found to have any two of the three scaled assessment criteria: serious, unanticipated, or study related, then timely reporting of the event needs to be made to the IRB office. If the problem event is found to have all three of the qualities serious, unanticipated, and study related, then an immediate report needs to be made to the IRE office. If the event is found to have only one or none of the qualities serious, unanticipated, or study related, then the problem event may be recorded for reporting to the IRB office at the time of continuing review.

* Immediate action, including one-time changes to approved study procedures may be taken to avoid apparent and immediate harm to subjects or others.

Reporting timeline

Problem events that should be reported in timely manner (**having 2** of any of the three qualities serious, unanticipated, or study related). Within **10 calendar days**.

Problem events that should be reported immediately (**having all three** of the qualities serious, unanticipated, and study related). Within **48 hours** of the occurrence.

Problem events that may be reported at the time of **continuing review** or study closure **having one or none** of the three qualities serious, unanticipated, or study related).

SOP 11.01 - Problems and Adverse Events, Record and Report

An initial problem report may take any form such as a phone call, email, excel spreadsheet, etc. but will eventually need to inform the IRB office in a formal manner where the event(s) are presented in a formal document with a date and acknowledgment from the Principal Investigator. The report should seek to:

- ▶ Provide a time line of the event(s),
- ▶ Discuss any steps or actions taken toward correcting the problem(s),
- ▶ Include a brief assessment from the Principal Investigator as to why the event(s) occurred,
- ▶ Include a brief assessment from the Principal Investigator as to whether or not a modification to current study procedures or alteration to the informed consent process is warranted.

3) Review

The ORI-RP and IRB when reviewing problem events, will consider the above classification system in conjunction with the formal problem event report to help determine the necessary level of review and action required to adequately address any concerns. In addition, the problem event(s) will be reviewed with consideration to 1) risk to subjects or others; 2) the overall study risk/benefit ratio; 3) the approved informed consent document; 4) whether the problem was anticipated or unanticipated involving risks to subjects or others, and 5) any possible need for the re-consent of current subjects, or to provide them with new information.

Problem events reported at any time other than the time of continuing review will be entered into the ORI-RP database as a study action requiring review concurrent with the previously established level of review for that study and or by an IRB Chair. If during the course of a problem event review, it is thought that a higher level of review of the event(s) is required, then arrangements will be made to obtain that review.

Unanticipated problems involving no more than minimal risk to subjects or others will be reviewed by a chair or designated reviewer in a timely manner.

Unanticipated problems involving risks to participants or others will receive immediate review by an IRB Chair to determine immediate course of action to protect subjects. The incident will be reviewed at the next convened board meeting or sooner. All documents pertaining to the event and the protocol will be distributed to all board members for review.

Promptly following IRB review of the event, a determination of an unanticipated problem involving risks to subjects or others, or serious or continuing noncompliance will be immediately reported to OHRP when the research is covered by DHHS regulations. When the research is not covered by DHHS regulations, written materials will specify that reports of unanticipated problems involving risks to participants or others are not to be report to OHRP. This report for an unanticipated problem involving risks to subjects or others will be sent to the FDA when the research is FDA-regulated. When research is not covered by the FDA regulations, written materials will specify that reports of unanticipated problems involving risks to subjects or others are not to be reported to the FDA.

Problem events reported at the time of continuing review will be considered reviewed in accordance with the rules and procedures established for continuing review. See SOP 5.10.

Some problems may require corrective action or additional consideration under the SOP governing researcher noncompliance. See SOP 11.02. If action is required from the IRB office beyond acknowledgment of the event(s), a formal letter will be issued to the Principal Investigator. Corrective action may include, but is not limited to,

- suspension or termination of IRB approval (convened IRB decisions only)
- a re-determination of the risk level of the study
- modification to an approved study procedure(s) and/ or the information provided during the consent process
- notification to current participants of relevant information



SOP 11.01 - Problems and Adverse Events, Record and Report

- reconfirming consent of current participants
- requiring additional monitoring for current and/ or past participants
- monitoring of the research (including audits) and/ or consent process
- education training, or mentoring for the principal investigator and/ or research team members
- modification to the continuing review schedule

4) Considerations for Additional Reporting

Where outside entities, or funding agencies/ sponsors are involved with the research, additional reporting of the event(s) and any subsequent actions may be required or desired and should seek to be made in a timely manner. PI's should consult with the IRB office prior to making a report to outside entities.

The appropriate regulatory agencies and organizational officials will be notified within 30 business days where any instance of unanticipated problems involving risks to subjects or others has been determined.

5. References

[OHRP Guidance on Reviewing and Reporting Unanticipated Problems involving risks to subjects or others:](https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html)

<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html>

[OHRP Guidance on Unanticipated Problems Involving Risks & Adverse Events Guidance \(2007\):](https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html)

<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html>

45 CFR 46.103(6)(5)

21 CFR 56.108(6)

[UNLV Rules and Procedures for Conducting Human Subjects Research](https://www.unlv.edu/policies/rules-and-procedures-conducting-human-subjects-research)

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