SOP 501: Unanticipated Problems

Terms and Abbreviations

Full board review: A review conducted at a convened meeting of the IRB at which a quorum of members is present
IO: Institutional Official; the individual who is legally authorized to act for the institution and ensures the effective functioning of the IRB
IRB: Institutional Review Board
IRB office staff: the IRB Manager, IRB Administrator, and any other IRB office staff, either collectively or individually
PI: Principal Investigator
Unanticipated Problems: Any problem occurring during the course of a research study that was not considered when the study was originally reviewed by the IRB.
UPIRSO: Unanticipated Problem Involving Risk to Subjects or Others

Overview

The IRB is responsible for monitoring the safety and welfare of human subjects. Part of this monitoring is ongoing review and assessment of Unanticipated Problems related to participation in the research. These may include adverse events, unexpected occurrences with the potential for harm, or subject complaints. (Protocol deviations and other types of noncompliance are treated separately in SOP 502: *Noncompliance*.)

Unanticipated Problems Involving Risks to Subjects or Others

Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs) are any occurrences during the conduct of a research study that result in harm, or that could result in harm if immediate action were not taken. The person harmed may be either a subject or others, i.e., someone else tangentially related to the research, such as research personnel or other individuals not directly part of the research. Specifically, an Unanticipated Problem is considered a UPIRSO if it meets all of the following criteria:

1. The event is 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. The event is 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. The occurrence 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.

Only Unanticipated Problems related to the research or possibly related to research must be reported. Related Unanticipated Problems occur as a result of:

- The interventions and interactions used in the research; or
- The collection of identifiable private information in the research.

Unanticipated Problems are *not* considered related and do *not* need to be reported to the IRB if they are the result of:

- An underlying disease, disorder, or condition of the subject; or
- Other circumstances unrelated to the research or any underlying disease, disorder, or condition of the subject.

The Principal Investigator must monitor and document the unanticipated problems related to the research throughout the life of the study. The PI must also evaluate whether the unanticipated problems are related to the research and what corrective actions should be implemented, if any, to prevent a similar occurrence in the future. If the reporting threshold is met, the PI must report the unanticipated problems to the IRB and implement corrective actions.

The PI is encouraged to consult with the IRB for questions or concerns related to unanticipated problems, or for assistance in determining whether the reporting threshold is met.

Study-Related Complaints

Unanticipated Problems may also take the form of complaints. While complaints typically are made by a research subject, they can originate with anyone who is aware of the research. Complaints may be made to the research team or directly to the IRB. Depending on the exact nature of the complaint, they may require immediate reporting to the IRB, or may be reported at the time of continuing review.

The PI is encouraged to consult with the IRB at any point for questions or concerns related to subject complaints, or for assistance in determining whether the reporting threshold is met.

Details and Procedures

Reporting

Subject deaths must be reported to the IRB within 24 hours. Otherwise, UPIRSOs must be reported to the IRB within 10 business days. The initial notification should be by phone or email to the IRB office, followed by the submission of a Reportable Event.

Unanticipated Problems that are not UPIRSOs must be reported within 10 business days via Reportable Event when, regardless of severity, the problem may alter the IRB's analysis of the study's risk to benefit ratio or where substantive changes in the research protocol or informed consent may be needed. Separate notification to the IRB office by phone or email is advised.

Examples:

Inclusion or exclusion criteria must be modified to mitigate a newly identified risk;

New monitoring procedures need to be implemented to ensure subject safety;

Study enrollment is halted due to the Unanticipated Problem;

Newly identified risks require notification to existing subjects and/or a modification to the informed consent.

All Unanticipated problems, both those that met immediate reporting requirements outlined above and any others that have been encountered, must be included in the annual Continuing Review or update summary to the IRB. If no Unanticipated Problems have occurred since the previous review, the researcher should state this.

Review Process

IRB office staff receive notification of an Unanticipated Problem and review the report to determine:

1. The effect of the Unanticipated Problem on the risk-benefit relationship of the research, (i.e., no change in risks or benefits; increased risks with no change in benefits; or increased risk and decreased benefits).
2. Whether the research protocol requires modifications.
3. Whether the informed consent process and/or informed consent document requires modification to inform currently enrolled subjects or subjects who have completed their research participation.
4. Whether frequency of continuing review should be increased.
5. Whether additional safeguards should be implemented to minimize risk and/or maximize the potential for benefit.

Depending on the nature and severity of the Unanticipated Problem, the IRB Office staff may consult with additional IRB members, the Chair, and/or the IO as needed, and may refer the Unanticipated Problem to the convened IRB.

The IRB office staff, Chair, and/or the IO may request that the Principal Investigator suspend research activities during the review process. However, only the Full Board may terminate the research.

Full Board IRB Review of an Unanticipated Problem

When an Unanticipated Problem is referred to the Full Board for review, it may be reviewed at the next regularly scheduled meeting or, if the matter requires special urgency, a special ad hoc meeting may be called.

The convened IRB may, at its discretion, implement any of the following actions:

- Acknowledge that the risk-benefit relationship has not changed and continue monitoring at the current continuing review interval.
- Request further information from the Principal Investigator.
- Require modifications to the research protocol and/or informed consent document.
- Require notification to currently enrolled subjects so they may decide whether they wish to continue participation.
- Require notification of subjects who have completed their participation in the research.
- Shorten the period of IRB approval (decreasing the time interval for continuing review reporting and IRB review).
- Implement additional safeguards (i.e., more frequent specific monitoring).

- Suspend enrollment of new subjects.
- Refer for further review as potential non-compliance.
- Terminate the research.
- Other actions deemed appropriate by the IRB. These actions must, however, be related to the research protocol(s) being evaluated. Actions related to researchers' employment or status are governed by University policies and are not in the IRB's purview.

The IRB office staff will notify the Principal Investigator in writing of the IRB's determination.

If the IRB determines that research activities should be suspended or terminated, IRB office staff will notify the IO. If appropriate, the IRB office staff or IO will notify the Sponsor, pertinent federal compliance offices, and internal University Administrators.

Subject Complaints

- If the IRB receives a complaint, IRB office staff will notify the PI that a complaint has occurred and provide relevant details, while keeping the identity of the individual making the complaint confidential. In some cases, it may be appropriate to reveal the identity of the complainant (e.g., if the complaint is related to subject payment, the identity may need to be revealed in order to issue compensation). This is done at the discretion of IRB office staff.
- If the PI receives a complaint that can be easily resolved, the appropriate action should be taken, an amendment submitted to the IRB if necessary, and the complaint reported at the next continuing review or annual update.
- If the PI receives a complaint that cannot be easily resolved or that involve a serious issue, this should be reported to the IRB as a Reportable Event within 10 business days. When in doubt, the PI may consult with IRB office staff to determine whether the complaint requires immediate reporting.

For all complaints:

1. IRB office staff will review the complaint and request additional information from the complainant and PI as needed.
2. IRB office staff work with the PI to determine the best way to resolve the issue, consulting with the Chair, other IRB members, and/or the IO as needed.
3. The PI may be required to submit an amendment if any study procedures or documents need to be modified as a result of the complaint.
4. For serious complaints, IRB office staff will notify the Chair and IO within 1 business day of receiving notification of the complaint.

   "Serious" is defined as a complaint that:

   - indicates serious noncompliance on the part of the investigator;
   - involves allegations of misconduct or illegal activity on the part of the investigator;
   - indicates that the risk-benefit ratio of the research may need to be re-assessed; or
   - requires prompt action by the IRB to resolve the complaint or mitigate potential harm.

References

45 CFR § 46.103(b)(5)

21 CFR § 56.108(b)(1)

Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events: OHRP Guidance (2007) https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html

SOP 502 *Noncompliance*

Revision History

Version	Date	Summary of Changes
1	1 Feb 2022	Initial version
	Click or tap to enter a date.	
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