

CUNY HRPP Policy: Unanticipated Problems and Adverse Events

1. Purpose

The purpose of this policy is to define unanticipated problems and adverse events associated with non-exempt human subject research, and to establish the reporting process and timeline for each.

2. Overview

Unanticipated problems and *adverse events* both involve undesirable experiences with the research protocol and/or subjects. Some unanticipated problems and adverse events may involve risks to subjects or others. These require prompt reporting to the IRB. Others can be reported at the time of continuing review.

3. What is an Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO)?

An unanticipated problem or an adverse event is considered to be an UPIRTSO when it meets ALL of the following criteria:

- a) It is **unexpected** (in terms of nature, severity, or frequency) given:
 - i. The research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and
 - ii. The characteristics of the subject population being studied;
- b) It is **related or possibly related** to participation in the research:
 - i. A UPIRTSO is related or possibly related to participation in the research when there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research; AND
- c) It 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.

4. What is an Adverse Event?

An adverse event is any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign, symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research. Examples include emotional distress, exacerbation of an existing mental disorder, a breach of confidentiality, or a complication from use of a medical device.

- a) An adverse event is considered a UPIRTSO when it meets ALL of the following three criteria:
 - i. The adverse event was **unexpected**. An unexpected adverse event is defined as any adverse event occurring in one or more subjects in a

research protocol, the nature, severity, or frequency of which is not consistent with either:

- The known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol-related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; OR
 - The expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.
- ii. The adverse event was **related or possibly related** to participation in the research. An adverse event is related or possibly related to the research when there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.
- iii. The adverse event places the subject or others at a greater risk of harm than was previously known or recognized. These adverse events fall in one of two categories:
- **Serious Adverse Event:** An adverse event is serious when medical or surgical intervention is required to prevent any of the following, or when any of the following occur:
 - Death
 - A life-threatening situation
 - Inpatient hospitalization
 - Prolongation of existing hospitalization
 - A persistent or significant disability/incapacity, or congenital anomaly/birth defect
 - **Life Threatening Adverse Event:** A situation or circumstance which places a subject at substantial risk of dying at the time of the problem; or the use or continuance of an intervention, a drug and/or a device that could possibly result in the death of a subject.

5. Reporting: UPIRTSOs Other Than Those Involving Subjects Deaths and/or Life Threatening Events

Unanticipated problems and adverse events, which meet all three criteria for UPIRTSOs, but which do not involve a subject death and/or life threatening event, must be reported to the IRB (and to sponsors and/or a central or independent monitoring committee [i.e. DSMB] as applicable) **within 5 working days**.

6. Reporting: Subject Deaths and Life Threatening Events

- a) The unanticipated death of a subject that is *related or possibly related* to the research must be reported to the IRB **within 24 hours**. If the cause of death is not available, this should not delay the report.
- b) An adverse event that is life threatening and *related or possibly related* to the research must be reported **within 24 hours**.
- c) Subject deaths that meet any of the following criteria must be reported to the IRB **at the time of continuing review**:
 - i. The death is due to the nature of the subject's underlying disease or condition, or is identified as due to a possible risk of the study procedure or intervention as described in the protocol and consent form;
 - ii. The death occurs more than 30 days after the subject stopped or completed all study procedures or interventions, or required research related follow-up;
 - iii. The death is that of a subject who did not complete the protocol for whatever reason, including voluntary withdrawal or removal by the PI;
 - iv. The death is that of a subject participating in a study which does not include a research intervention (for example, an observational study tracking outcomes).

7. Reporting: Other Unanticipated Problems and Adverse Events

Unanticipated problems and adverse events that do not require prompt reporting to the UI-IRB (per criteria defined in Sections 4 and 5 of this Policy) must be submitted as a summary of events at continuing review.

8. Principal Investigator Responsibilities

When reporting unanticipated problems and adverse events, the Principal Investigator shall assess the cause and seriousness of the event and advise whether:

- a) A change in the protocol is necessary to minimize the risks to subjects;
- b) The consent form should be revised to reflect the risk, and/or
- c) Subjects previously enrolled in the study should be re-consented in light of the risk(s).

9. Authority to Review

9.1. Review by CUNY Administration

- a) If immediate risks to subjects are involved, the University Director for Research Compliance or his/her designee, in consultation with the Vice Chancellor for Research and/or UI-IRB Chair, may take one or more actions prior to IRB review which may include (but are not limited to):
 - i. Immediate suspension of human subject research activities to ensure the ongoing safety of subjects;
 - ii. Request additional information from the Principal Investigator or others;
 - iii. Refer the report to a UI-IRB Chair or Vice Chair for review;
 - iv. Convene an emergency meeting of the UI-IRB, or a UI-IRB subcommittee, to review the report.
- b) The principal investigator shall be promptly notified in writing of the determination and any required steps for corrective action.
- c) All actions taken by CUNY Administration shall be promptly reported to the convened UI-IRB for review.

9.2. Review by an IRB Chair or his/her Designee

- a) A UI-IRB Chair or his/her designee may review events where only slight changes in risk have been reported, such that only minor changes in the study protocol or informed consent documents are required. The UI-IRB Chair or his/her designee may ask investigators and/or Data Safety Monitoring Boards or others for additional clarifying information and may require corrective actions.
- b) The principal investigator shall be promptly notified in writing of the UI-IRB Chair or his/her designee's determination, and any required steps for corrective action.
- c) Any suspensions shall be reported to the convened UI-IRB in accordance with CUNY Policy.

8.3. Review by a Convened IRB

- a) A convened UI-IRB or a UI-IRB subcommittee must review UPIRTSOs and adverse events that meet the criteria for reporting within 24 hours or 5 days.
- b) The principal investigator shall be promptly notified in writing of the IRB's determination, and any required steps for corrective action or termination.

8.4. Corrective Actions

Corrective actions that may be required by either the convened UI-IRB or the UI-IRB Chair or his/her designee include (but are not limited to):

- a) Modifying the inclusion or exclusion criteria to mitigate the newly identified risks;
- b) Implementing additional monitoring procedures of subjects;
- c) Modifying informed consent documents to include a description of newly recognized risks;
- d) Revising the protocol;
- e) Providing additional information about newly recognized risks to previously enrolled subjects;
- f) Suspending enrollment of new subjects;
- g) Suspending approval of the research;
- h) Termination of the research *(Only the convened UI-IRB or the Institutional Official can make this determination.)*

10. External Reporting Requirements

The Office of the Vice Chancellor for Research will promptly communicate in writing to federal agencies and/or sponsor(s), as required, the details and corrective actions related to the UPIRTSO(s).

10.1. Information to be included in the report:

- a) Name of the CUNY institution(s) conducting the research;
- b) Title of the research project and/or grant proposal in which the UPIRTSO(s) occurred;
- c) Name of the principal investigator on the protocol;
- d) Number of the research project assigned by the IRB and the number of any applicable sponsored program or project;
- e) A detailed description of the UPIRTSO(s); and
- f) Any additional pertinent details related to the UPIRTSO(s), including corrective actions

References

1. [Code of Federal Regulations, Title 45 – Public Welfare DHHS, Part 46 – Protection of Human Subjects](#)
2. [U.S. Department of Health & Human Services. Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events. January 15, 2007.](#)