

Human Research Protection Policy

SUBJECT: Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events

Unanticipated Problems Involving Risks to Subjects or Others

1. Unanticipated problems involving risks to subjects or others (**hereinafter referred to as unanticipated problems**) are defined as any incident, experience, or outcome that meets all of the following criteria:
 - (a) 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;
 - (b) 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
 - (c) 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.
2. EXAMPLE of an unanticipated problem:
 - (a) A PI conducts a survey of college students that collects individually identifiable sensitive information about illicit drug use and other illegal behaviors. The data are stored on a laptop computer without encryption and the laptop is stolen from the PI's office. This is an unanticipated problem that must be reported.
3. The IRB requires prompt reporting of any events that may represent unanticipated problems. All reports should be made by contacting the Office of Research Compliance as soon as the researcher becomes aware of the event, but in all cases within 10 business days.

Adverse Events

1. An adverse event is any injury, trauma, or illness experienced by a subject that required medical or psychological intervention or treatment.
2. An **unexpected adverse event** is any adverse event occurring in one or more subjects participating in a research protocol, the nature, severity, or frequency of which is **not consistent** with either:
 - (1) 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



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IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or

- (2) 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.

3. A **serious adverse event** is any adverse event that:

- (1) results in death;
- (2) is life-threatening (places the subject at immediate risk of death from the event as it occurred);
- (3) results in inpatient hospitalization or prolongation of existing hospitalization;
- (4) results in a persistent or significant disability/incapacity;
- (5) results in a congenital anomaly/birth defect; or
- (6) based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed above.

4. EXAMPLE of an adverse event:

- a) A PI conducts a detailed survey of college students that involves questions about early childhood experiences. The research was evaluated as involving no more than minimal risk and was approved by an IRB member under an expedited review procedure. During completion of the survey, one participant has a transient psychological reaction manifested by intense sadness and depressed mood that resolved without intervention after a few hours. The PI had not anticipated such a reaction and therefore the protocol and informed consent document did not describe this type of risk. Although not serious, this adverse event must be reported.

5. Adverse events must be reported by the PI or a member of the research team using the IRB Protocol Adverse Event Reporting Form (<http://www.mu.edu/researchcompliance/research/irbforms.shtml>). Any serious adverse event must be reported within 24 hours of the researcher becoming aware of the event. All other adverse events must be reported as soon as the researcher becomes aware of the event, but in all cases within 5 business days.

Unanticipated Problem and Adverse Event Review

1. The PI must report any events that may represent unanticipated problems or adverse events (**collectively referred to as unanticipated problems**) in accordance with the policy as set forth above.
2. Reported unanticipated problems are reviewed by a member of the Office of Research Compliance. The ORC may request clarifications or further information from the PI to



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properly evaluate the occurrence. The IRB Chair or Vice Chair may be consulted at any time during this review process.

3. If the ORC determines that the occurrence is not an unanticipated problem, the PI's report is acknowledged as submitted and the PI is notified that the occurrence is not considered an unanticipated problem involving risks to subjects or others and no further action is needed.
4. If the ORC determines that the occurrence may be an unanticipated problem, the occurrence is referred to the convened IRB for review, with an evaluation and recommendation from the ORC. The IRB Chair or Vice Chair will serve as the primary reviewer.
5. The convened IRB evaluates the occurrence by considering whether it is an unanticipated problem and makes a final determination via vote by a quorum of the IRB.
6. If the IRB determines that the occurrence is not an unanticipated problem, the PI's report is acknowledged as submitted and the PI is notified that the occurrence is not considered an unanticipated problem involving risks to subjects or others and no further action is needed.
7. If the IRB determines that the occurrence is an unanticipated problem, the actions that may be taken include, but are not limited to the following:
 - (a) The PI is required to submit a protocol amendment.
 - (b) The PI is required to amend the informed consent form.
 - (c) The PI and/or the PI's staff are required to participate in additional training/education for the protection of human subjects in research.
 - (d) The PI is required to develop and submit for IRB approval a Data and Safety Monitoring Plan.
 - (e) The PI is required to submit periodic status reports.
 - (f) The protocol requires IRB review more frequently than once per year.
 - (g) The PI is required to provide current subjects with additional information if it might affect their decision to continue participation in the research.
 - (h) The PI is required to provide additional information to previously enrolled subjects.
 - (i) The PI is required to re-consent currently enrolled subjects.
 - (j) The PI is required to notify investigators at other research sites.
 - (k) Some or all of the research protocol may be suspended or terminated.
 - (l) The data must be destroyed and may not be used when reporting the research results.