

Unexpected Problem Checklist for PI's

***How to determine what needs to be reported to the IRBs and what actions to take regarding unexpected adverse events and problems that place participants or others at greater risk**

If the occurrence is reported as an adverse reaction (adverse event according to FDA/OHRP), it is considered unexpected when **all** of the following criteria are met:

1. When an adverse reaction occurs in one or more subjects participating in research where the nature, severity or frequency of the event is not consistent with:
 - Known or foreseeable risk of events associated with the procedures involved in the research and described in the protocol documents, investigator's brochure, and current informed consent document and other relevant sources of information such as product labeling or inserts;
 - The expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the reaction and their predisposing risk factor profile for the adverse event.

2. The adverse reaction is considered related or probably (possibly according to OHRP guidance) related when the event is determined to be at least partially caused by the procedures involved in the research
 - If an event is determined to be solely caused by underlying disease, disorders, or conditions of the participant or other circumstances unrelated to either the research or any underlying disease, then is it **not** considered related.

3. The adverse reaction meets any of the following criteria:
 - Results in death
 - Is life threatening (places the participant at immediate risk of death from the event as it occurred)
 - Results in inpatient hospitalization or prolongation of existing hospitalization
 - Results in persistent or significant disability/incapacity
 - Results in a congenital anomaly/birth defect, or
 - Based upon medical judgments, may jeopardize the participant's health and may require medical or surgical intervention to prevent one of the outcomes listed in this definition

The unexpected event meets **all** of the following required criteria:

1. Unexpected in terms of nature, severity, or frequency given the procedures described in the research protocol and the characteristics of the subject population being studied.
2. Related or probably related to participation in research (probably related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.
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.

Immediate action is necessary when there is an adverse reaction or unexpected event to protect the safety, welfare, or rights of participants or others. **At least one** of the following actions must be taken:

- eliminating the immediate hazard
- termination of the research
- suspension of research procedures in currently enrolled subjects
- suspension of enrollment of new participants
- modification of inclusion or exclusion criteria
- modification of informed consent documents to include newly recognized risks
- additional information about the risks to previously enrolled participants will be required

For multi-site studies, there is an adequate plan to communicate information (i.e., data safety monitoring committee) among the sites because the event may affect the health or safety of the participants or their willingness to continue to participate in the study.