University of Central Oklahoma
Institutional Review Board

GUIDANCE ON REPORTING UNANTICIPATED PROBLEMS AND ADVERSE EVENTS

Definitions

Adverse Event: Any untoward or unfavorable occurrence in a human subject, including any abnormal sign (e.g., laboratory findings), 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. [Modified from the definition of adverse events in the 1996 International Conference on Harmonization E-6 Guidelines for Good Clinical Practice.]

Possibly related to the research: There is a reasonable possibility that the adverse event, incident, experience or outcome may have been caused by the procedures involved in the research. [Modified from the definition of associated with use of the drug in FED regulations at 21 CFR 312.32(a)]

Serious Adverse Event: Any adverse event temporally associated with the subject’s participation in research that meets any of the following criteria:
1. results in death;
2. is life-threatening (places the subject at immediate risk of death from the event as it occurred);
3. requires inpatient hospitalization or prolongation of existing hospitalization;
4. results in persistent or significant disability/incapacity;
5. results in congenital anomaly/birth defect; or
6. any other adverse event that, 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 in this definition.
[Modified from the definition of serious adverse drug experience in FDA regulations at 21 CFR 312.32(a)].

Unanticipated problem involving risks to subjects or others: Any incident, experience, or outcome that meets all of the following criteria:
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 a subject’s participation 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) related to the research than was previously recognized.
**Unexpected adverse event**: 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:

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 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.

(Expected or anticipated adverse events are those listed in the approved study documents such as the consent form, approved protocol, etc.)

[Modified from the definition of serious adverse drug experience in FDA regulations at 21 CFR 312.32(a)].

**Helpful Questions to Ask:**

1. Is the event 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. Is the event 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

3. Does the event suggest 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?

*If the answer to all three (3) questions is “Yes”, the event is considered an Unanticipated Problem and must be reported to the IRB within five (5) business days of the investigator or the investigative staff’s learning of the event. The report should be made using the Report of Unanticipated Problems form.*

*If the event involves a possibly related, life threatening experience or death, it must be reported to the IRB within 48 hours of the investigative staff learning of the event. Note: the event must meet all 3 criteria above.*

A record should be kept of all study related (or possibly study related) adverse events and unexpected problems (see above for definitions). At the time of continuing review or study closure, a summary report should be submitted to the IRB.

If the “related to study” or “expected severity or frequency” evaluation of an event or problem changes such that all 3 criteria are met, a report should be made to the IRB within 5 business days.