

Oregon Public Health Division
PH Institutional Review Board

Unanticipated Problem/Adverse Event Report

The review and reporting of unanticipated problems (UAP) and adverse events (AE) are to occur in a timely, meaningful way so that human subjects can be better protected from avoidable harm while reducing unnecessary burden. Only a small subset of adverse events are unanticipated problems that must be reported under 45 CFR 46. Please complete this form in alignment with the PHD [Reports of Unanticipated Problems and Adverse Events](#) guidance document.

Principal Investigator:		Phone:	
		E-mail	
Title of Research Project:		Funding Source:	
IRB Study No.:	IRB Approval Expiration Date <i>(n/a for studies that no longer require continuing reviews)</i>		
The study is (check one):	<input type="checkbox"/> Currently in progress (open to enrollment) No. of subjects enrolled: No. of subjects still in treatment: <input type="checkbox"/> Closed to enrollment (participants in follow-up or data analysis only)		
Date of Event:			
Date of awareness of event:	<p><i>Fatal or potentially life-threatening incidents, experiences, or outcomes must be reported to the PH IRB within 5 working days after the research team becomes aware. If applicable and this report is being submitted to the PH IRB > 5 days post awareness, explain why:</i></p> <p><i>All other unexpected incidents, experiences, or outcomes must be reported to the PH IRB within 15 working days of the research team becoming aware. If applicable and this report is being submitted to the PH IRB > 15 days post awareness, explain why:</i></p>		
Description of Event: (give a detailed report and specific pertinent information)			

Below, identify the incident, experience, or outcome as either an adverse event, an adverse event that must be reported as an unanticipated problem, or an unanticipated problem that is not an adverse event. If you need assistance in determining the correct selection, please see flow charts below and note the PH IRB will review this form and request revisions as found necessary.

<input type="checkbox"/> Adverse Event (AE)	<p>Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign, symptom, or disease, temporally associated with the individual's participation in the research, whether or not considered related to the subject's participation in the research. Such events are reasonably anticipated to occur as a result of the study procedures or participation or are part of the normal disease progression and should thus be described in the research proposal and informed consent document. This includes <u>both physical and psychological harm</u> and occurs most commonly in the context of biomedical research.</p> <p><i>Does NOT need to be reported to OHRP under the HHS regulations at 45 CFR 46, however, if required under the monitoring provisions described in the IRB-approved protocol, the adverse event must be reported to a monitoring entity (e.g., research sponsor, the coordinating center, or a DSMB) as this entity may subsequently determine that the AE does in fact represent an unanticipated problem.</i></p>
<input type="checkbox"/> An AE that is an Unanticipated Problem <p><i>* The vast majority of AE's occurring in human subjects are <u>not</u> unanticipated problems.</i></p>	<p>The AE is <u>all of the following</u>: unexpected, related/possibly related to participation in the research, <u>and</u> suggests that the research places subjects or others at a greater risk of harm than was previously known/recognized.</p> <p>*Guidance on assessing whether an AE should be reported as an UAP can be found below.</p> <p><i>Per 45 CFR 46, must be reported to the supporting HHS agency head and OHRP.</i></p>
<input type="checkbox"/> Unanticipated Problem (UAP) <i>(not related to AE)</i>	<p>The UAP is <u>all of the following</u>: Unexpected, related or possibly related to participation in the research, <u>and</u> suggests that the research places subjects or others at a greater risk of harm (<u>including physical, psychological, economic, or social harms</u>) than was previously known/recognized.</p> <p><i>Per 45 CFR 46, must be reported to the supporting HHS agency head and OHRP.</i></p>

Description of any and all steps and actions taken in response to the incident or to resolve the issue:

Number of similar experiences in this protocol:

What was subject(s) participation level after the event?

- | | |
|---|---|
| <input type="checkbox"/> Stopped research participation | <input type="checkbox"/> Subject(s) had already completed research intervention |
| <input type="checkbox"/> Continued research participation | <input type="checkbox"/> Subject(s) withdrew from further participation |
| <input type="checkbox"/> Continued participation/follow-up only | <input type="checkbox"/> Investigator withdrew subject(s) from participation |
| <input type="checkbox"/> Other (describe): | |

Effect on Research – In your judgment, should the research:

continue as planned with no changes to the research protocol or consent process. Explain why:

continue with changes to the research protocol or consent process; *Attach red-lined proposed changes for PH IRB review and approval. If more than minor, the changes must be reviewed and approved by our convened IRB.*

Provide a summary of these changes here:

suspend new subject enrollment until the event is further examined; or

be terminated (stopped completely), with all subjects removed from research.

Does this study have a Data Safety Monitoring Board (DSMB)? Yes No

If yes, has the DSMB been notified? Yes No
(If Yes, provide the PH IRB with a copy of this report)

If required under the monitoring provisions described in the IRB-approved protocol, this must be reported to the relevant monitoring entity (e.g. research sponsor, the coordinating center, or a DSMB).

Have other agencies or sponsors been notified of this event? Note, typically the PH IRB is responsible for reporting unanticipated problems to the supporting HHS Agency head and OHRP. Per PH IRB Policy, regardless of funding, all unanticipated problems will be reported to OHRP.

Yes (list agencies/sponsors notified and send a copy of relevant reports to the PH IRB):

No. List your supporting Agency:

- v. 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.

***Adverse events that are unexpected, related or possibly related to participation in research, and serious are the most important subset of AE's representing UAP's as they always suggest greater risk of physical or psychological harm than was previously recognized and routinely warrant consideration of substantive changes in the protocol, informed consent process, or other corrective actions in order to protect the safety, welfare, or rights of subjects.*

- b. Or, does the event not meet the above definitions of "serious" but still suggests that subjects or others are at a greater risk of physical or psychological harm than was previously recognized?

Corrective actions or substantive changes that may need to be considered in response to an UAP:

- Change to protocol initiated by the P.I. prior to obtaining IRB approval to eliminate apparent immediate hazards to subjects;
- Modification of inclusion/exclusion criteria to mitigate newly identified risks;
- Implementation of additional procedures for monitoring subjects;
- Suspension of enrollment of new subjects or suspension of research procedures in currently enrolled subjects;
- Modification of informed consent documents to include a description of newly recognized risks; and
- Provision of additional information about newly recognized risks to previously enrolled subjects.

**The flow chart below provides an algorithm for determining whether an AE represents an UAP that needs to be reported under HHS regulations at 45 CFR 46.

Unanticipated Problem Analysis

Box 1

Any AE may be considered unexpected if it occurs in one or more subjects, the nature, severity, or frequency of which is not consistent with either:

- o the known or foreseeable risk of AEs 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
- o 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.

Box 2

Adverse Events may be caused by one or more of the following:

- 1) The procedures involved in the research;
- 2) An underlying disease, disorder, or condition of the subject; or
- 3) Other circumstances unrelated to either the research or any underlying disease, disorder, or condition of the subject.

In general, AEs that are determined to be at least partially caused by (1) would be considered related to participation in the research, whereas adverse events determined to be solely caused by (2) or (3) would be considered unrelated to participation in the research.

An adverse event occurs in one or more subjects.

1) Is the adverse event unexpected in nature, severity, or frequency?
(See Box 1)

YES

2) Is the adverse event related or possibly related to participation in the research?
(See Box 2)

YES

3) Does the adverse event suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized? NOTE: If the adverse event is serious, the answer is always "YES."

YES



Report the adverse event as an unanticipated problem under 45 CFR 46



The adverse event is not an unanticipated problem and need not be reported under 45 CFR 46

NO

NO

NO