SOUTHERN ILLINOIS UNIVERSITY CARBONDALE

Institutional Review Board Policy

IRB Policy #:	**280**
Policy Title:	***Adverse Events and Unanticipated Problems***
Date Approved:	
Date Reviewed:	

Purpose: To define responses necessary to report and remediate adverse events and unanticipated problems during research.

Policy:

Unanticipated Problems

Events or problems that are unfavorable, harmful, or detrimental to the welfare of study subjects or other individuals involved with a research study AND that meet all the following criteria are unanticipated problems (45 CFR 46.103(b)(5)):

1. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures 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
3. suggests that the research places subjects or others at a great risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or recognized

Adverse Events

Adverse events are not defined by Federal regulations. OHRP uses the term adverse event very broadly and includes any event meeting the following definition:
Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the participant'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).

Adverse events encompass both physical and psychological harm. They occur most commonly in the context of biomedical research, although on occasion they can occur in the context of social and behavioral research. They may be caused by one or more of the following: a) the procedures involved in the research; b) an underlying disease, disorder, or condition of the subject; or c) other circumstances unrelated to the research or any underlying disease, disorder or condition of the subject.

What Needs to be Reported to the IRB:
Adverse events that are NOT unanticipated problems do not need to be reported to the IRB. This means that the approved IRB protocol clearly specified the risks involved in the study and the adverse event was anticipated. Therefore, research participants were aware of the possibility of the adverse event occurring.

If, however, an adverse event occurs that was not anticipated, then the PI must report the adverse event to the IRB. The following questions may help determine whether the adverse event was unanticipated:

1. Is the adverse event unexpected? An unexpected adverse event is any adverse event that is not known or foreseeable as is described in the research protocol or other related sources of information or is not consistent with 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.
2. Is the adverse event related to or possibly related to participation in the research? Possibly related to means there is a reasonable possibility that the adverse event may have been caused by the procedures involved in the research.
3. Does the adverse event suggest that the research places the subjects or others at a greater risk for harm than was previously known or recognized? (NOTE: If an adverse event is serious then the answer is always "yes.") To determine whether this criterion is met, first determine whether the adverse event is serious. That is, does it result in death, a life-threatening condition, hospitalization, disability/incapacity, congenital abnormality or birth defect, or medical intervention (surgery)? Also determine whether the research participants are placed at greater risk for experiencing physical or psychological concern than what was anticipated. If it is not serious, it still may require changes to the protocol.

All unanticipated problems must be promptly reported to the IRB and any other monitoring entity (e.g. department chair, sponsor). If the unanticipated problem is *serious* then the PI must report it to the IRB within one (1) week of its occurrence. Any other unanticipated problem should be reported to the IRB within two (2) weeks of its occurrence. All unanticipated problems should be reported to the DHHS (if the research is federally-funded) and the sponsor (if applicable) within one month of the IRB's receipt of the PI's report of the problem.

Research investigators are responsible for reporting to both subjects and to the IRB significant findings developed in the course of the research that may relate to the subject's willingness to

continue participation whether they qualify as unanticipated problems or adverse events or not.

Examples
The case study below is an example of an unanticipated problem that must be reported under the DHHS regulations.

An investigator conducting behavioral research collects individually identifiable sensitive information about illicit drug use and other illegal behaviors by surveying college students. The data are stored on a laptop computer without encryption, and the laptop computer is stolen from the investigator's car on the way home from work. This is an unanticipated (but not adverse event) problem that must be reported because the incident was (a) unexpected (i.e., the investigators did not anticipate the theft); (b) related to participation in the research; and (c) placed the subjects at a greater risk of psychological and social harm from the breach in confidentiality of the study data than was previously known or recognized.

An example of an adverse event that does not include unanticipated problems and does not need to be reported under 45 CFR §46 follows:
An investigator is conducting a psychology study evaluating the factors that affect reaction times in response to auditory stimuli. In order to perform the reaction time measurements, subjects are placed in a small, windowless soundproof booth and asked to wear headphones. The IRB-approved protocol and informed consent document describe claustrophobic reactions as one of the risks of the research. The twentieth subject enrolled in the research experiences significant claustrophobia, resulting in the subject withdrawing from the research. This example is not an unanticipated problem because the occurrence of the claustrophobic reactions – in terms of nature, severity, and frequency – was expected

The following is an example of an adverse event with an unanticipated problem that must be reported in the context of social and behavioral research because, although not serious, the adverse event was (a) unexpected; (b) related to participation in the research; and (c) suggested that the research places subjects at a greater risk of psychological harm than was previously known or recognized.
A behavioral researcher conducts a study in college students that involves completion of a detailed survey asking questions about early childhood experiences. The research was judged to involve no more than minimal risk and was approved by the IRB chairperson under an expedited review procedure.
During the completion of the survey, one student subject has a transient psychological reaction manifested by intense sadness and depressed mood that resolved without intervention after a few hours. The protocol and informed consent document for the research did not describe any

risk of such negative psychological reactions. Upon further evaluation, the investigator determines that the subject's negative psychological reaction resulted from certain survey questions that triggered repressed memories of physical abuse as a child. The investigator had not expected that such reactions would be triggered by the survey questions. In this example, the adverse event warranted consideration of substantive changes in the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare or rights of subjects.

The IRB chair and/or the convened IRB will review reports of any adverse events or unanticipated problems involving risks to subjects or others. Upon receipt of a report of an unexpected serious harm, the IRB will determine whether more detailed information is required, whether the study should be suspended or terminated and will report this to the Vice Chancellor for Research for review. If necessary, the Vice Chancellor for Research will report this to the Department of Health and Human Services (DHHS).

With the receipt of a report of an unexpected event that is not serious, the IRB may suggest a modification to the procedures to reduce the level of risk to subjects, or may require a modification to the consent form to include a description of the event. Any subsequent modification by the PI must be reviewed and approved by the IRB before implementation. Examples of corrective actions or substantive changes that might need to be considered in response to an unanticipated problem include:

1. changes to the research protocol initiated by the investigator prior to obtaining IRB approval to eliminate apparent immediate hazards to subjects
2. implementation of additional procedures for monitoring subjects
3. suspension of enrollment of new subjects
4. suspension of research procedures in currently enrolled subjects
5. modification of informed consent documents to include a description of newly recognized risks
6. provision of additional information about newly recognized risks to previously enrolled subjects