Adverse Events Reporting

Pepperdine Investigator's Duties and Responsibilities to Report Unanticipated Problems Involving Risk to Participants or Others and Protocol Violations

Pepperdine student, faculty and staff Investigators must report adverse events that occur during the course of their research with human subjects to the IRB in a timely fashion. An adverse event, as defined by the Department of Health and Human Services, is "an undesirable and unintended, although not necessarily unexpected, result of therapy or other intervention." An adverse event in non-medical research can include an undesirable and unintended consequence of, or reaction to, procedures. An unanticipated adverse event can also be defined as any adverse experience whose nature, severity, and frequency of risk were not described in the information provided for IRB review or in the consent form.

The Three Criteria to Identify an Unanticipated Problem

The Department of Health and Human Services Office of Human Subjects Protections considers unanticipated problems, in general, to include 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 participation in the research** (in this guidance document, 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. 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.

The Two Types of Unanticipated Problems

An unanticipated problem may be either one of two types:

- **Type 1:** Potential harm
- **Type 2** : Actual harm

A "*potential harm*," a type 1 'unanticipated problem', is an issue that must be reported to the IRB whenever something comes to an investigator's attention regarding the research which indicates the **possibility** that previously unsuspected harm may occur (or may occur at a higher than expected rate) even though no one has yet experienced actual harm. It is an event, development, or information that potentially increases the likelihood of harm occurring in the future.

A type 2 '*unanticipated problem*' is a recognized harmful or unfavorable outcome that has actually occurred to a research subject, a set of subjects, another individual being treated in a similar fashion in a relevant non-research setting, or another person connected to the research study (e.g. one of the researchers or the spouse of a subject).

This type of unanticipated problem is an actual event(s) not a potential risk. These kinds of unanticipated problems are *also* Adverse Events (AEs). A series of AEs that signal the AEs were not just isolated occurrences and were significant to subjects' rights and welfare would be considered an *unanticipated problem*. An expected AE that occurs at a greater frequency or severity than expected would be an unanticipated problem. 'Type 2' unanticipated problems should be reported to the Pepperdine Graduate & Professional Schools or Seaver IRB using the Adverse Event Reporting Form (attach) and also in **Eprotocol (give hyperlink)**.

'Seriousness' and Unanticipated Problems

An unanticipated problem because it is associated with potential risks is a problem that must be reported even if it is not felt to be serious. Adverse events that are unexpected and related, but *not* serious, would also be unanticipated problems if they suggest that the research places

'Others' and Unanticipated Problems

Although the primary mission of an IRB is to protect the rights and welfare of research subjects, federal regulations require investigators to report, and IRBs to evaluate, any unanticipated problem that may pose risks to people who are not the actual research subjects. The 'others' are most often the researchers themselves or family members of the subjects, although they can be people not associated with the research in any way. If a research subject experienced an unexpected side effect like fainting, and fainted while driving a car, causing an accident in which a stranger was injured, this would be an unanticipated problem even if the subject was unharmed.

Internal and External Unanticipated Problem

Investigators are required to report both internal and external unanticipated problems to the IRB.

An internal 'Pepperdine' unanticipated problem is one that occurs during a study that was approved by either the Graduate & Professional Schools or Seaver IRB and involves a Pepperdine faculty, student or staff member. The unanticipated problem may occur anywhere in the United States or internationally and may or may not involve human subjects. When such an unanticipated problem occurs this is considered a 'Pepperdine' event and must be reported to the appropriate campus IRB.

An "unanticipated problem" that occurs during a study which is *not* under the primary oversight but involves Pepperdine investigators, which was approved by an '**External**' IRB, a non-Pepperdine IRB is still an "unanticipated problem." These unanticipated problems should be reported to either Graduate & Professional Schools or Seaver IRB and the 'External' IRB which approved the study.

When reporting an internal or external “unanticipated problem,” an investigator(s) must complete and submit a hardcopy Pepperdine IRB Adverse Events Reporting Form (attach) to the IRB and also submit an Adverse Report in eProtocol.

Federal Government’s Oversight of Research and Protections of Human Subjects

The Department of Health and Human Services Office of Human Research Protections (OHRP) regulations require IRBs “have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others, or any serious or continuing non-compliance with this policy or the requirements or determinations of the IRB and (ii) any suspension or termination of IRB approval.” 45 CFR 46.103(b)(5)

Examples of Unanticipated Problems

Examples of Procedures that could cause or be linked to an unanticipated problem	***Examples of Unanticipated Problems Involving Procedures***
• Surgery required as part of the research • Storage of research data on computers or in medical records • Disclosure of genetic tests results • Completion of a survey	**Type 1—Potential Harm:** Newly published studies involving the heart surgery procedure in monkeys and chimps show an increased risk of early heart failure. **Type 2—Actual Harm:** A subject is denied life-insurance coverage because of a genetic test conducted solely for the purposes of the research study. **Type 2—Actual Harm:** Completed surveys about illegal drug use by a company's employees are accidentally left behind by a researcher and turned in to employees' supervisors by the janitorial staff.
Examples of Non-Procedural events or information that could cause or be linked to an unanticipated problem	***Examples of Unanticipated Problems Involving Non-Procedural Events or Information***
• Article in a journal • Internet security breach	**Type 1—Potential Harm:** FDA adds additional risks to a drug that is being used on label as part of a study. **Type 1 —Potential Harm:** An article in JAMA indicates that women with diabetes have a previously

	unknown risk of developing heart disease when taking the drug used in a research study (where having diabetes is not an exclusion criteria for the study) **Type 2—Actual Harm:** Hackers break into an internet site used by subjects to report progress in weight management. Names and contact information are stolen and sold to companies that market illegal diet drugs through email.
Examples of Persons that could cause or be linked to an unanticipated problem	***Examples of Unanticipated Problems Involving Persons in the Research***
• Subject/participant • Investigator • Lab personnel	**Type 1—Potential Harm:** It is discovered that the study coordinator forged case report forms and falsified the results of blood tests that had been conducted for subject safety. **Type 2—Actual Harm:** A research subject holds the research team and other subjects hostage at gunpoint when he learns he received the placebo drug.