



UNIVERSITY OF CALIFORNIA, SAN DIEGO
HUMAN RESEARCH PROTECTIONS PROGRAM

FACT SHEET

**Reporting Unanticipated Problems Involving Risk to Participants
or Others (UPRs) to the IRB**

A. Overview

1. Investigators often engage in a popular strategy of over-reporting and relying upon the IRB triage mechanisms for deciding what reports go to convened meetings.
2. OHRP notes that because most individual adverse events (AEs) do not appear to represent unanticipated problems, the vast majority of AEs do not need to be reported to the IRB.
3. UCSD's HRPP has revised its Standard Operating Policies and Procedures in response to recent guidance published by OHRP and FDA.
4. This document is intended to guide Principal Investigators and research staff when reporting unanticipated problems or adverse events to the IRB.

B. Regulatory Background

1. Federal regulations [45CFR46.103(b)(5) and 21CFR56.108(b)(1)] require the IRB to ensure that investigators promptly report "any unanticipated problems involving risk to subjects or others" (UPR). UPRs are defined by OHRP as any problem or event, which in the opinion of the Principal Investigator was: 1) unanticipated, 2) serious, AND 3) at least possibly related to the research procedures.
2. The OHRP document entitled "Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events" dated January 15, 2007 can be found at the [Office for Human Research Protections \(OHRP\) Website.](#)

C. What To Report

1. The following events meet the definition of UPR and should be reported to an IRB within 10 working days:
 - a. Any serious event (including injuries, side effects, deaths or other problems) that in the opinion of the Principal

- Investigator was unanticipated, involved risk to subjects or others, and was at least possibly related to the research procedures.
- b. Any serious accidental or unintentional change to the IRB-approved protocol that alters the level of risk.
 - c. Any deviation from the protocol taken without prior IRB review to eliminate apparent immediate hazard to a research subject.
 - d. Any new information (e.g. publication, safety monitoring report, updated sponsor safety report), interim result or other finding that indicates an unexpected change to the risk/benefit ratio of the research.
 - e. Any breach in confidentiality that may involve risk to the subject or others.
 - f. Any complaint of a subject that indicates an unanticipated risk or that cannot be resolved by the Principal Investigator.
2. The question of whether the event involved hospitalization, serious injury, or death is no longer of primary relevance in determining what should be reported.
 3. If the event meets all 3 criteria for a UPR as defined above in B.1, it must be reported to the IRB within 10 working days.
 4. When a subject injury occurs that is directly related to study and medical costs are incurred (regardless if the event was anticipated or a UPR), the Investigator must notify Clinical Research Billing. Reporting instructions are located on the [Clinical Research Billing site](#). Note: This site is on the Intranet and is a secure site for UCSD employees only.
 5. A [decision tree](#) is available on this website to guide the Principal Investigator and research staff when reporting UPRs to the IRB.

D. Definitions

1. **Unanticipated (unexpected) problems/events** are those that are *not* already described as potential risks in the consent form, *not* listed in the Investigator's Brochure or *not* part of an underlying disease. Anticipated (expected) problems/events do NOT meet the definition of UPRs.
2. **Serious problems/events** are those, which in the opinion of the Principal Investigator involve risk to subjects or others. Examples may include death, hospitalization, disability as well as breach of confidentiality. Non-serious problems/events do NOT meet the definition of UPRs.
3. A **Serious Adverse Event** is defined by the FDA as any adverse drug experience occurring at any dose that results in any of the

following outcomes: death, a life-threatening adverse drug experience, inpatient hospitalization, or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. FDA Regulations require IND sponsors to report serious AEs via expedited reporting.

4. Problems/events that are unanticipated and serious should be reported to the IRB within 10 working days *only* if in the opinion of the Principal Investigator they are possibly, probably or definitely related to the research procedures. Those serious, unanticipated problems/events that the Principal Investigator deems unlikely or not related do NOT meet the definition of UPRs and need not to be reported to the IRB.

E. Reporting Internal (on-site) UPRs to the IRB

1. Follow-up reports on previous events should be reported as UPRs if the initial event itself met the definition of UPR AND in the Principal Investigator's judgment, this follow-up report adds value to the initial report.
2. For reports involving blinded study drug, the assessment of relatedness will often be "at least possibly related" as relatedness cannot always be ruled out.
3. For reasons of confidentiality, subject names must not be included in any UPR reports. Subject identifiers such as enrollment numbers should be used instead. Do NOT include signed informed consent documents with the report of an UPR to the IRB.
4. Investigators may have AE reporting requirements (e.g., to an industry sponsor, the FDA or the NIH) in addition to IRB reporting requirements. ***It is the investigator's responsibility to know and comply with these additional requirements.***
5. PIs are encouraged to submit UPR reports using paper format. Use the currently approved [UPR reporting form](#). Hard copy submissions ensure that there is no information lost which can happen when uploading the report electronically and that the report can always be submitted over the PI's signature. Once the HRPP office receives the hard copy, it will be scanned into the study file and made available to all relevant research oversight offices.
6. When a subject injury occurs that is directly related to study and medical costs are incurred (regardless if the event was anticipated or a UPR), the Investigator must notify Clinical Research Billing.

F. Reporting External (off-site) UPRs to the IRB

1. Only when a particular adverse event or series of adverse events is determined to meet the criteria for an unanticipated problem should a report of the adverse event(s) be submitted to the IRB under the HHS regulations at 45 CFR part 46.103 (b)(5).
2. Reports of off-site events on studies that are now closed at this site should be reported as UPRs if the event meets the definition of UPRs AND in the Principal Investigator's judgment, this event might affect risk to subjects who have completed the study.
3. The local PI serves as the recipient of the external (off-site) reports. The PI must provide a summary report to the IRB within 10 working days of receiving the off-site report that includes:
 - a. A clear explanation of why the adverse event or series of adverse events has been determined to be an unanticipated problem.
 - b. The investigator should review the report and assess whether it identifies the adverse event as being: (1) unexpected; (2) related or possibly related to participation in the research; and (3) serious or otherwise one that suggests that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized.
 - c. A description of any proposed protocol changes or other corrective actions to be taken by the investigators in response to the unanticipated problem should be described. (For example, whether these reports require any modifications to approved recruitment materials, consent forms, or research plans.)
4. The HRPP office will not send notification to the PI that these reports were received.
5. The PI is required to maintain reports as agreed upon with the sponsor and following institutional policy.

G. Reporting Problems or Events That Do Not Qualify As UPRs

1. All problems/events that do NOT meet the definition of a UPR should be reported to the IRB in summary form (using a table or spreadsheet) at the time of annual continuing review. Accompanying documentation (sponsor report forms, etc.) need NOT be included with this summary.
2. When a subject injury occurs that is directly related to study and medical costs are incurred (regardless if the event was anticipated or a UPR), the Investigator must notify Clinical Research Billing.