

Stanford University HRPP Policy Guidance	Events and Information that Require Prompt Reporting to the IRB	GUI-P13 1/3
--	--	----------------

Scope

This guidance applies to all non-exempt human subject research. It explains events or circumstances that must be **promptly** reported to the IRB during the conduct of human subject research. "Prompt reporting" is done using the Report Form in [eProtocol](#).

This guidance covers:

- Events and information which require prompt reporting to the IRB:
 - 1) Unanticipated problems involving risks to participants or others ("UPs")
 - 2)–6) New information, protocol deviation or violation (such as possible noncompliance), complaint, participant incarceration, unanticipated adverse device effect (UADE)
 - 7) Other events or information where "prompt reporting" is not required
- [More guidance on UPs](#)
- [How to submit a report; Timeframes](#) – all studies including cancer, CTRU, and VA studies.

Events and information which require prompt reporting to the IRB

1) Unanticipated Problems Involving Risks to Participants or Others (UPs)

Events (internal or external, deaths, life-threatening experiences, injuries, breaches of confidentiality, or other) occurring during or after the research study, which in the opinion of the Monitoring Entity or the PD meet **all** of the following criteria:

a) Unexpected

in terms of nature, severity, or frequency, given (a) the research procedures described in the protocol-related documents, and (b) the characteristics of the subject population being studied;

AND

b) Related to participation in the research

or there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research;

AND

c) Harmful

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.

NOTE:

- A "UP" generally will warrant 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 or others.
- **Devices:** If event is associated with a device, report under item 6) UADE.

2) New Information that indicates a change to the risks or potential benefits of the research in terms of severity or frequency (e.g., analysis indicates lower-than-expected response rate or a more severe or frequent side effect; other research finds arm of study has no therapeutic value; FDA labeling change or withdrawal from market)

3) Protocol Violation or Deviation, only if:

- Intended to eliminate apparent immediate hazard to a research participant, or
- Harmful (caused harm to participants or others, or placed them at increased risk of harm - including physical, psychological, economic, or social harm), or
- Possible serious or continued noncompliance.

4) Complaint unresolved by the research team, or that indicates increased or unexpected risks.

5) Incarceration when in the opinion of the PD it is in the best interest of the participant to remain on the study.

6) Unanticipated adverse device effect (UADE)

Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects. [21 CFR 812.3\(s\)](#)
[More guidance on UADE](#)

7) Other events or information

Examples include major deficiencies identified in audits, and VA Local SAEs.

Report only after consulting with IRB Education (650-724-7141; IRBeducation@stanford.edu).

More guidance on UPs

➤ **Unexpected**

protocol-related documents refer to the IRB-approved research protocol, informed consent document, investigator brochure, protocol, package insert, or label.

characteristics of the subject population being studied refer to 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.

➤ **Related to participation in the research** or there is a reasonable possibility

In general if event is determined to be caused:

- at least partially by the procedures involved in the research it would be considered **related** to participation in the research;
- solely by an underlying disease, disorder, or condition of the subject, or other circumstances unrelated to either the research or any underlying disease, disorder, or condition of the subject it would be considered **unrelated** to participation in the research.

➤ **Harmful**

[Adverse events](#) need not be "serious" to qualify as "harmful". However, "serious adverse events" always meet the "Harmful" criterion.

- **Serious adverse event** is defined by OHRP as an event that:
 - (1) results in death;
 - (2) is life-threatening (places the subject at immediate risk of death from the event as it occurred);
 - (3) results in inpatient hospitalization or prolongation of existing hospitalization;
 - (4) results in a persistent or significant disability/incapacity;
 - (5) results in a congenital anomaly/birth defect; or
 - (6) 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
- **"Not serious" adverse events might also be UPs:** adverse events that are not serious would also be unanticipated problems if they suggest that the research places subjects or others at a greater risk of physical, psychological, economic, or social harm than was previously known or recognized.

FDA-regulated drug studies: See definitions in FDA regulations at [21 CFR 312.32\(a\)](#).

Stanford University HRPP Policy Guidance	Events and Information that Require Prompt Reporting to the IRB	GUI-P13 3/3
--	--	----------------

How to Submit a Report; Timeframes

- **Submit to IRB** using [eProtocol](https://eprotocol.stanford.edu/irb) Report Form (<https://eprotocol.stanford.edu/irb>)
 - **Timeframe for UP reports depends on Monitoring Entity**
Report an unanticipated problem involving risks to participants or others (UP or Internal Events that are unexpected and related to the research) **within 10 working days***, ******:
 - **If PD is the only monitoring entity**
Items 1 - 6 should be reported **directly** to the IRB **within 10 working days** from when the PD learns of the event or new information.
 - **If there is a monitoring entity in addition to, or other than, the PD**
Report to the IRB using this form **within 10 working days** from receiving assessment from monitoring entity. Only when an event has been assessed by the monitoring entity to be a UP should the PD report it to the IRB.
 - **Timeframe for Reportable Information (items 2 - 6)**
These should always be reported by the PD **directly** to the IRB **within 10 working days** from when the PD learns of the event or new information.
- * Unexpected deaths or life-threatening experiences related to the research (at Stanford, or when STANFORD is the coordinating institution in a multi-site study) must be reported to the IRB **within 5 working days** from PD learning of event.
- ** **VA Studies:** Report "serious unanticipated problems" **within 5 business days** of becoming aware of them. See [VHA Handbook 1058.01](#) for definitions of *serious unanticipated problems*, and *unanticipated SAEs*. For possible additional requirements, contact the VA Human Protections Administrator, at 650-493-5000, ext. 67593.
- **Additional Reporting**
 - **Cancer Studies (including CTRU cancer studies)** - Use the CCTO Adverse Event Communication Form to report the event to Stanford Cancer Center according to Cancer Center [Standard Operating Procedures](#).
 - **CTRU Study "only" (not Cancer Study):** Submit a report to CTRU Nurse Manager, M/C: 5706.

Resources: Regulations and Guidance	
OHRP	<ul style="list-style-type: none"> • 45 CFR 46.103 (b)(5) • Reviewing and Reporting UPs Involving Risks to Subjects or Others and Adverse Events - Guidance
FDA	<ul style="list-style-type: none"> • 21CFR 812.150 Investigational Device – reports • 21 CFR 312.32(a) Investigational New Drug – safety reports • Adverse Event Reporting to IRBs - Improving Human Subject Protection - Guidance
Resources: Other References	
Stanford HRPP	<ul style="list-style-type: none"> • Ch 3.10 Unanticipated Problems Involving Risks to Participants or Others (UPs), and Other Reportable Information • Unanticipated Adverse Device Effect (UADE) [GUI-P14]