An event involving research conduct and/or a research participant

1. **Is the event an Adverse Event (AE)?**
   - Yes
     - **Is the event unexpected?**
       - Yes
         - **Is the event related?**
           - Yes
             - Are participants or others placed at greater risk?**
               - Yes
                 - Report to IRB promptly as an Unanticipated Problem (UP).
               - No
                 - **Report in IRB annual & final reports.**
             - No
               - **Are participants or others placed at greater risk?**
                 - Yes
                   - Report to IRB promptly as an Unanticipated Problem (UP).
                 - No
                   - **Report in IRB annual & final reports.**
     - No
       - **Report in IRB annual & final reports.**

2. **Does the event involve risk to study participants or others?**
   - Yes
     - **Are participants or others placed at greater risk?**
       - Yes
         - Report to IRB promptly as an Unanticipated Problem (UP).
       - No
         - **Report in IRB annual & final reports.**
   - No
     - **Report in IRB annual & final reports.**

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Please note that participant or other complaints must also be reported promptly to the IRB.

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An unanticipated problem (UP) can be an AE in a trial participant or an event that is not considered an AE affecting a trial participant or others. Here are a few examples:

**Ex1: UP that is an AE**
A participant in a trial testing a new hip replacement device experiences hip swelling more severe than described in documents.
- Unexpected (severity not described in protocol or accompanying documents)
- Related to participation in research
- Placed participants at greater risk of physical harm

**Ex2: UP affecting participants that is not an AE**
An investigator conducting research collects individually identifiable sensitive information about illicit drug use by surveying college students. The data are stored on a laptop computer without encryption, and the laptop is stolen from the investigator’s car.
- Unexpected (theft not anticipated)
- Related to participation in the research
- Placed the participants at a greater risk of psychological/social harm

**Ex3: UP affecting others that is not an AE**
A research team conducting interviews draws gunfire at field site, with a bullet hitting a spouse of a participant and a research coordinator.
- Unexpected (gunfire was not anticipated)
- Related to research conduct
- Placed participants and others (participants’ family members and research personnel) at a greater risk of physical and psychological harm
**Adverse Event (AE):** Any untoward medical occurrence associated with the use of a medical product in humans, whether or not considered medical product.

*21 CFR 312.32 & 21 CFR 803.3*

**Others:** Persons who are not participants in the trial, but are affected by the trial. Examples include the participants’ sexual partners, participants’ family members, research personnel, and anyone else as applicable.

*HHS Unanticipated Problems Involving Risks & Adverse Events Guidance (2007) & UCSD IRB:*

https://irb.ucsd.edu/Decision_tree_UPRs.pdf

**Unexpected:** Any research event occurring in one or more participants or others involved in a research protocol, the nature, severity, or frequency of which is not consistent with either: the known or foreseeable risk of research events 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 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.

*HHS Unanticipated Problems Involving Risks & Adverse Events Guidance (2007)*

**Related:** Any research event related or possibly related (there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research) to participation or role in the research.

*HHS Unanticipated Problems Involving Risks & Adverse Events Guidance (2007).*


**Greater Risk:** Any risk where research places participants or others are at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

*HHS Unanticipated Problems Involving Risks & Adverse Events Guidance (2007)*

**Unanticipated Problem (UP):** Any incident, experience, or outcome that meets all of the following criteria: unexpected, related, and greater risk. UPs from externals sites must also be reported to by internal site investigator to internal site IRB promptly.

**Promptly:** Term not defined by CFR. Refer to your specific IRB requirements. For example USC IRB requires reporting of UP reporting within 10 calendar days.

*HHS Unanticipated Problems Involving Risks & Adverse Events Guidance (2007) & 45 CFR 46.103(b)(5)*