**Adverse Event (AE) Reporting**

Any AE must be reported in **Case Report Forms (CRFs)** per sponsor guidelines.

- **Device (IDE)**
  - *Sponsor* reports any AEs that affect the risk analysis for SRDs to FDA at least yearly.
  - Is it a **Unanticipated Adverse Device Effect (UADE)**?
    - Yes: Investigator reports to sponsor and IRB per sponsor/IRB guidelines. Usually within 10 working days.
    - No: *Sponsor* reports to FDA, all reviewing IRBs and participating investigators within 10 working days.

- **Drugs (IND)**
  - **Sponsor** reports all AEs to FDA annually within 60 days of the IND effective date.
  - Is it a **serious adverse event (SAE)**?
    - Yes: Investigator reports to sponsor per sponsor guidelines. Usually within 24-48 hours of learning of the AE.
    - No: Is it **Unexpected**?
      - Yes: Yes/Probably Yes
      - No: Is it **Suspected**?
        - Yes: Yes/Probably Yes
        - No: Is it fatal/life threatening?
          - Yes: **Sponsor** reports to the FDA within 15 calendar days.
          - No: **Sponsor** reports to the FDA within 7 calendar days.
**Adverse Event (AE) Reporting Definitions**

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**Significant Risk Device (SRD):** an investigational device that:

1. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
2. Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
3. Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
4. Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

21 CFR 812.3

**UADE: Unanticipated Adverse Device Effect:** 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 & 21 CFR 812.150

**SAR: Suspected Adverse Reaction:** Any adverse event for which there is a reasonable possibility that the drug caused the adverse event. For the purposes of IND safety reporting, “reasonable possibility” means there is evidence to suggest a causal relationship between the drug and the adverse event.

21 CFR 312.32

**SUSAR: Suspected Unexpected Serious Adverse Reaction Reporting:** Not fatal or life-threatening, sponsor must report to FDA within 15 calendar days. 21 CFR 312.32

Reporting: Fatal or life-threatening, sponsor must report to FDA within 7 calendar days. 21 CFR 312.32

**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

- the protocol–related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and
- 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)

**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. There may be additional safety reporting requirements for sponsors who hold INDs to report to the FDA within 15 calendar days. These may include

- an aggregate analysis of specific events observed in a clinical trial (such as known consequences of the underlying disease or condition under investigation or other events that commonly occur in the study population independent of drug therapy) that indicates those events occur more frequently in the drug treatment group than in a concurrent or historical control group,
- findings from other studies,
- findings from animal or in vitro testing, or
- increased rate of occurrence of serious suspected adverse reactions.

21 CFR 312.32