Adverse Event Module
Part 1: Definitions

Agenda
• Define adverse event (AE)
• Define serious adverse event (SAE)
• Define life-threatening event
• Define unexpected adverse event
• Define suspected adverse reaction (SAR)
• Define unexpected adverse device effect (UADE)

Summary Definition
Any unwanted sign, symptom, or disease that was not seen before individual's research participation, or worsening of baseline symptom, REGARDLESS OF EXPECTEDNESS OR RELATIONSHIP TO RESEARCH.
Alias Clinical Terms

- Toxicity
- Side effect
- Acute or late effect
- Complication
- Adverse drug reaction
- Adverse drug event

Purposes of Adverse Event Monitoring

- Identify events that may have immediate effect on the safety of the participant
- Inform regulators, investigators, and others of new and important information about events
- Provide a summary of adverse experiences in order to develop the drug or regimen toxicity profile

OHRP AE Definition

*Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events*

*“Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research.”*
FDA AE Definition

21 CFR 312.32 (a)

• “Any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related.”

FDA Related AE Definitions

• FDA regulations use different terms when referring to an adverse event.
  • Adverse effect (21 CFR 312.64)
  • Adverse experience (21 CFR 312.32)
  • Adverse reactions /adverse event (used interchangeably in 21 CFR 312.32)
  • Unanticipated problems (21 CFR 312.66)

ICH GCP AE Definition

• “Any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.”
### Additional Definitions

- Serious
- Life-threatening
- Unexpected
- Suspected Adverse Reaction (SAR)
- Unanticipated Adverse Device Effect (UADE)

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**Serious Adverse Event (SAE)**

**21 CFR 312.32, ICH GCP, OHRP Guidance**

Any AE occurring at any dose that results in any of the following outcomes:

- Death
- Life-threatening adverse drug experience
- Inpatient hospitalization or prolongation of existing hospitalization
- Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- Congenital anomaly/birth defect

OR...

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**...Serious Adverse Event (SAE)**

**21 CFR 312.32, ICH GCP, OHRP Guidance**

- Important medical events (IME) that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate 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.
**Life-Threatening**

*21 CFR 312.32, ICH GCP*

- An adverse event or suspected adverse reaction is considered "life-threatening" if, in the view of either the investigator or sponsor, its occurrence places the patient or subject at immediate risk of death.

**FDA Definition: Unexpected**

*21 CFR 312.32 (a)*

- Not listed in the investigator brochure (IB)
- Not listed at the specificity or severity that has been observed
- If no IB, not consistent with the risk information described in the general investigational plan or elsewhere in the current IND application
- If mentioned in the IB as occurring with the drug class or anticipated based on the pharmacological properties of the drug, but are not specifically mentioned in the IB

**OHRP & ICH GCP Definition:**

**Unexpected AE**

**OHRP Guidance:**
Adverse event that is not described in terms of nature, severity, or frequency given:
- the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document, and
- the characteristics of the subject population being studied

**ICH GCP:**
Adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., IB for an unapproved investigational product or package insert/summary of product characteristics for an approved product).
Suspected Adverse Reaction (SAR)  
21 CFR 312.32

- Any AE for which there is a reasonable possibility that the drug caused the AE
- Reasonable possibility means there is evidence to suggest a causal relationship between the drug and AE

Unanticipated Adverse Device Effect (UADE)  
21 CFR 812.3(s)

- “Any serious adverse effect on health or safety, 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 application; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.”

Summary

- Adverse Event
  - Any unwanted sign, symptom, or disease that was not seen before individual's research participation, or worsening of baseline symptom, REGARDLESS OF EXPECTEDNESS OR RELATIONSHIP TO RESEARCH.
- Serious
- Life-threatening
- Unexpected
- Suspected Adverse Reaction
- Unanticipated Adverse Device Effect