



Drug Safety and Adverse Events for Clinical Trials: An Introduction

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Proper processing and reporting of Adverse Events (AE) during a clinical trial are critical components of Good Clinical Practice (GCP). This article takes a lifecycle approach to this subject matter content by reviewing how to define Adverse Events and Serious Adverse Events (SAE), characteristics, types of Adverse Events, defining roles and responsibilities in managing adverse events, through to FDA reporting requirements for Serious Adverse Events.

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“...Adverse Events (AE) in patients participating in clinical trials must be reported to the local Institutional Review Board (IRB) and the study sponsor by the clinical investigator. Adverse events categorized as serious (for example, death, illness requiring hospitalization, events deemed life-threatening, or involving cancer, or fetal exposure) must be reported to the FDA immediately; whereas minor adverse events are simply documented in the annual summary sent to the regulatory authority.

The sponsor collects AE reports from the clinical investigation sites, and notifies all participating sites of the AEs reported, together with both the clinical investigators' and the sponsor's judgment of the seriousness of the AEs. This process allows the sponsor and all the clinical investigators access to a set of data that might suggest potential problems with the study treatment while the study is still ongoing.

Eliminating Apparent Adverse Events

The following are examples of situations and events that would not be classified as AEs: (See FDA Guidance for Clinical Investigators, Sponsors, and IRBs: Adverse Event Reporting to IRBs Improving Human Subject Protection.)

- A medical or surgical procedure (e.g., endoscopy, appendectomy, etc.), although the condition that leads to the procedure is an AE
- Anticipated day-to-day fluctuations of preexisting diseases or conditions (including laboratory values) present or detected at the start of the study that do not worsen
- The disease or disorder being studied, or expected progression, signs, or symptoms of the disease or disorder being studied, unless they become more severe or occur with a greater frequency than expected for the subject's condition

Defining Roles and Responsibilities in the Management of Adverse Events

Types of Adverse Events

All clinical trials have the potential to produce adverse events. AEs are classified as serious or minor; expected or unexpected; and study-related, possibly study-related, or not study-related. For example, during a clinical study that is designed to evaluate the safety and effectiveness of an investigational drug, the potential exists for study subjects to experience an adverse event, such as a rash. However, subjects in that study



could also have a fatal reaction to the clinical trial experimental drug treatment. Both the outbreak of a rash and a sudden death would be considered AEs. In this case, the rash would be classified as minor, unexpected, and possibly study-related. The death would be classified as serious and unexpected. The principal investigator at the clinical investigation site would use his or her medical judgment to determine whether the death could have been related to the study drug. This is referred to as assigning causality.

Both the rash and the death are unexpected events, and should alert the clinical researcher to the existence of a potential problem with the new experimental drug. The principal investigator at the clinical research site is required to report these AEs to the local IRB and to the sponsor, and await direction on whether to stop the study. Moreover, if the principal investigator determines that there is imminent danger posed by the new experimental pharmaceutical, he or she can use medical discretion to prohibit further subjects from participating in the study..."

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