Adverse Event (AE) Reporting and Evaluation

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Disclaimer

The information herein is not intended to replace any in-depth personal review of the Code of Federal Regulations, ICH GCP Guidelines, or any other applicable IRB, federal, state, or local rules, laws, or guidelines applicable to the conduct of clinical research at this investigative site.
Objective

Upon completion of this module, you will be able to:

- Describe the identification, assessment, follow-up, and reporting of adverse events and serious adverse events.
Adverse Event (AE)

What is an Adverse Event (AE)?

An AE is any unfavorable and unintended change in the structure (signs), function (symptoms), or chemistry (lab data) of the body temporally associated with the use of the sponsor’s product, whether or not considered related to the use of the product.
Adverse Experience (AE)

An adverse experience can be:

- Symptom
- Physical Exam finding
- Syndrome or disease
- Abnormal laboratory value
- Worsening of a pre-existing condition
Serious Adverse Event (SAE)

Any adverse drug experience occurring at any dose that results in any of the following outcomes:

- Death
- Life-threatening adverse drug experience
- In-patient hospitalization or prolongation of existing hospitalization
- Persistent or significant disability/ incapacity
Serious Adverse Event
continued

Any adverse drug experience occurring at any dose that results in any of the following outcomes:

- Congenital anomaly/ birth defect
- Important medical events
- Cancer
- Overdose
Clinical History

How do we know it’s an AE?

- Medical history
- Pre-existing conditions
  - A clinical condition which is diagnosed prior to enrollment is a pre-existing condition and should be documented as part of a subject’s medical history
  - When assessing for adverse experiences, the subject’s medical history should be reviewed for pre-existing conditions
Clinical History

Continued

Always ask the Subject:

- How have you felt since your last visit?
- What other medications have you used?
- Have you seen any other health care providers?
Investigator - definitions and responsibilities

- Principal Investigator (PI)
  - a person responsible for the conduct of the clinical trial site

- Sub-investigator
  - an individual member of the clinical team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or make trial-related decisions
Physician Investigator Assessment

“A qualified physician, who is an Principal Investigator or a Subinvestigator for the trial, should be responsible for all trial-related medical decisions.”
Physician Investigator Assessment

continued

- Includes timely review of:
  - All laboratory data
  - All adverse experiences
Physician Investigator Assessment
continued

- Maximum Intensity
  - mild
  - moderate
  - severe

- Duration

- Action taken

- Relationship to test drug
Unblinding of drug treatment

- Treatment should not be unblinded except under emergency conditions
- Emergency unblinding procedures are described in the protocol
- Unblinding should be discussed with the sponsor if possible
- Safety of the subject is paramount
Documentation of Adverse Events

- Description of experience
- Onset, duration & date of resolution
- Intensity of experience
- SAE or AE
- MD /DO assessment of causality
- Treatment or action taken
- Outcome
Documentation of Serious Adverse Events continued

- Obtain all source documentation:
  - Hospital admission, discharge summaries, and notes
  - Procedure reports
  - Laboratory and medication data

- All relevant documents should be completed and forwarded to appropriate sponsor representative
Reportable Adverse Events from Clinical Studies

- Serious Adverse Experiences (SAEs)
- Adverse Events (AEs)
- AEs that occur during screening process after informed consent has been signed
- AEs that occur within designated time period after last dose of study
- Use during pregnancy or lactation (whether or not associated with an adverse event)
All data should be reviewed for possible AEs and consistent terminology should be used throughout all sections.
## Adverse Experience Reporting

### Time Frames for Reporting AEs Originating from Clinical Studies:

<table>
<thead>
<tr>
<th></th>
<th>Sponsor</th>
<th>IRB</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Serious AEs</td>
<td>Via telephone</td>
<td>Within 5 days</td>
</tr>
<tr>
<td></td>
<td>within 24 hours</td>
<td></td>
</tr>
<tr>
<td>All AEs</td>
<td>Via CRF only</td>
<td>At renewal</td>
</tr>
</tbody>
</table>

[Link]
IND Safety Reports

- Report submitted to FDA & all participating investigators of adverse experience associated with the use of the drug that is both serious & unexpected
- expeditious reporting required
IND Safety Reports continued

- Medically-qualified investigator must review
- Copy sent to IRB
- File in investigator binder
Summary

- Identification & reporting of adverse experiences is crucial.
- SAEs must be reported to sponsor within 24 hours of the site’s knowledge of the experience.
- Sites must follow IRB requirements for reporting adverse experiences & IND safety reports.
- Medically-qualified investigators must assess causality for all adverse experiences.