Adverse Event (AE) Reporting

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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 should be able to describe:

- What an Adverse Event is
- How to recognize an AE
- Assessment & Follow-up
- Reporting responsibilities
Adverse Experience (AE)

Any untoward medical occurrence in a patient or a clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. [ICH 1.2]
Adverse Event (AE)

Any untoward medical occurrence in a patient or a clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. [ICH 1.2]

“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.” [OHRP]
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 untoward medical occurrence that at any dose results in:

- Death
- Is Life-threatening
- Requires In-patient hospitalization or prolongation of existing hospitalization
- Persistent or significant disability/ incapacity
Serious Adverse Event: continued

Any untoward medical occurrence that at any dose results in:

- Congenital anomaly/ birth defect
- Important medical events
Clinical history

- 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)

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?
Physician Investigator Assessment

“A qualified physician, who is an Investigator or Sub-investigator for the trial, should be responsible for all trial-related medical decisions”.

[ICH 4.3.1]
Investigator definitions

- **Investigator**
  - 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

(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 NSAE
- PI 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 Events (SAEs)
- Non-Serious Adverse Events (NSAEs)
- 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)
Adverse Event Reporting (continued)

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:

- All SAEs: Via telephone within 24 hours
- All Non-Serious AEs: Via CRF/Workbook
- IRB: as per SOPs
UC Davis IRB Reporting

- AEs are reported in Table format at annual renewal submission
- SAEs occurring at UCD site
- **AND**
- Related, Serious, &/or other unanticipated problem
- Within 5 days of becoming aware of event
provided that all four of the following criteria are met:

1. occurred at UC Davis; and

2. suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized; and

3. is unanticipated; and

4. is related or possibly related to the research
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 required.
- 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 and relatedness for all adverse experiences.
Helpful Websites

ICH GCP Guidelines (E6 Efficacy)


FDA Code of Federal Regulations Title 21

Helpful Websites

UCD IRB SOP for Reporting AE & Other Unanticipated Problems

UCD IRB Form – Report of AEs & Other Unanticipated Problems
Questions???

Thank You!