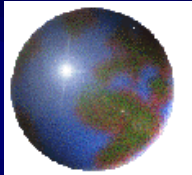


The Fundamentals of International Clinical Research Workshop



Understanding Adverse Events

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What is an Adverse Event?

- An AE is *any* untoward medical occurrence in a subject undergoing a study related procedure and believed reasonably to be caused by that study related procedure.
 - *DMID Greater than Minimal Risk protocol template*

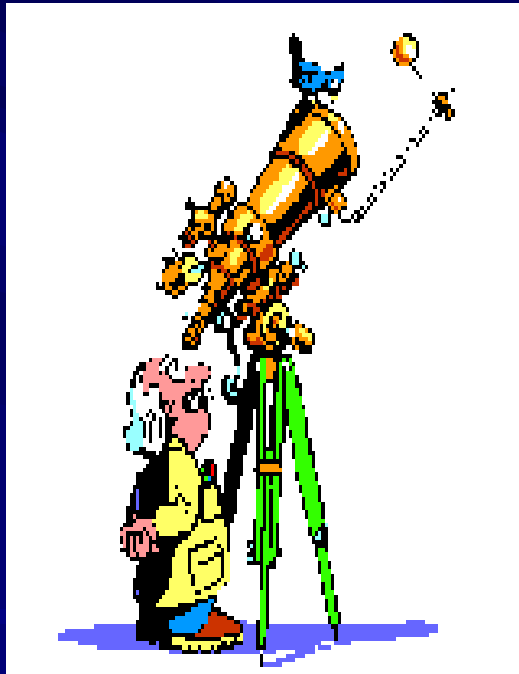
Reason for Adverse Event Collection and Reporting

- **The most important responsibilities of investigators and sponsors of clinical research studies:**
 - Protection of study participants.
 - Collection of accurate and reproducible data.
- **All clinical studies greater than minimal risk must have an AE collection and reporting system in place.**

Do Not Ignore Safety



Detecting Adverse Events



- Symptoms
(headache, nausea)
- Syndromes of disease
- Physical findings
(elevated BP, lump)
- Abnormal lab values
- Pregnancy
- Behavioral changes
- Toxicities

How Would You Describe an AE?

- **Wherever possible, describe AE in terms of a change in the status or diagnosis, NOT the symptoms.**
- **Example: “decrease in Hb from 10.1 to 7.3”**
- **Example: “influenza” rather than stomach cramps, fever, chills.**

Assess Severity of the AE

- AEs assessed by the investigator using protocol defined grading system
- If protocol has no defined grading system, use guidelines such as Toxicity Tables
- The protocol or Toxicity Tables will define what values or findings are considered abnormal

Assess Relatedness of AE

- In a clinical study the study product or procedure must always be suspect.
 - Is there a *reasonable* possibility that the AE may have been caused by the investigational product/intervention?
 - NO- not reasonably associated
 - YES- possibly associated



What Is a Serious Adverse Event?

- Death
- Congenital anomaly or birth defect
- Permanent Disability
- Hospitalization or prolongation of hospitalization
- Life threatening (at immediate risk of death)
- Condition that requires medical or surgical intervention to prevent one of the above

Serious vs Severe

- **Serious:**
“Serious AE” is a regulatory definition (21 CFR 312.32)
- **Severe:**
Severe is defined as an intensity classification (mild, moderate, severe)

Severe AE ≠ Serious AE

What happens when an AE is identified?

- Ensure a qualified physician who is an investigator is responsible for medical decisions
- Provide appropriate medical care to participant
- Gather all source documents: lab reports, x-rays, hospital records, etc.
- Complete AE case report form & SAE form if needed
- Follow-up until resolved or stabilized
- Report according to study requirements.

Documentation of AE

- Adverse Event Case Report Form
- SAE report form if needed
- Source documents
- ALL must match and be complete
- Principal Investigator (or other designated investigator) must sign SAE report
- Report to sponsor and IRB as required.

Design study to reduce risks

- Weigh the risks and benefits of all study activities
- Consider possible AEs when developing inclusion/exclusion criteria
- Include Safety Labs and Safety Assessments
- Build in follow-up procedures
- Search for AEs
- Consult with DMID

Protocol Development

State explicitly in the protocol:

- Known risks and possible AEs
- If assessing pre-existing conditions and concomitant meds
- Timeline for detecting and reporting AEs
- How severity and relationship assessed—if using Toxicity Table or other resources
- Reporting plans—who does what when

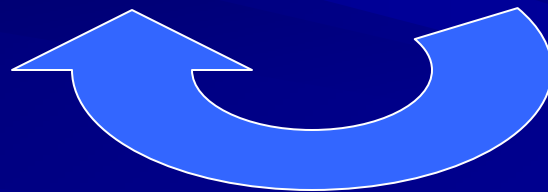
Safety Vigilance

Design for safety



Identify Safety
Issues

Execute
protocol



AE Summary

- Define in protocol all procedures for detecting and reporting AEs.
- PI or designated clinician must assess intensity and relatedness
- Treat AEs based on best clinical practice available
- Ensure source documentation, CRFs and SAE form match
- Design protocol for participant safety

Appendix:

SAMPLE Adverse Event Form

Study Name: _____

ADVERSE EVENT FORM

1. Study Number.....	_ _ _ _ _ _ _	_ _ _ _
2. Center Number.....	_ _ _ _ _ _ _	_ _ _ _
3. Participant Number.....	_ _ _ _ _ _ _	_ _ _ _
4. Date of Contact.....	_ _ _ / _ _ _ / _ _ _ _ _	month day year
5. Diagnosis: _____		
6. Date of AE onset:.....	_ _ _ / _ _ _ / _ _ _ _ _	month day year
7. Related to study product?.....	_ _	
1= yes		
2= no		
8. Was the AE serious? (0=no; 1=yes).....	_ _	
<i>If yes, complete the Serious Adverse Event Form and notify FHI immediately.</i>		
9. Highest severity of AE during the study.....	_ _	
1=mild		
2=moderate		
3=severe		
10. Was the AE treated? (0=no; 1=yes).....	_ _	
<i>If yes, complete Concomitant Therapy Form.</i>		
11. Outcome of AE.....	_ _	
1=resolved without sequelae		
2=resolved with sequelae → <i>specify sequelae</i> _____		
3=AE still present at study completion/discontinuation		
4=participant died as a result of this AE		
5=unknown because participant could not be located		
12. Date of resolution or death.....	_ _ _ / _ _ _ / _ _ _ _ _	month day year
*Serious means:	<p style="text-align: center;">FOR FHI USE ONLY</p> <p>Was the AE anticipated? _ _ </p> <p> 0=no</p> <p> 1=yes</p>	
<ul style="list-style-type: none"> • life threatening or fatal • resulted in significant/persistent disability or incapacity • resulted in hospitalization or prolongation of hospitalization • congenital anomaly in an infant • jeopardized participant and required medical/surgical intervention to prevent serious outcome • any other event that the investigator considered serious 		

Initials of person completing form

Date of form completion