

POLICIES AND PROCEDURES

SECTION: Research and Compliance			NUMBER: CLN-35.00	
CHAPTER: Clinical Research Standard Operating Procedures	ISSUED: 7/28/2008	REV. A: 4/11/2009	REV. B: 9/1/2010	REV. C:
TITLE: Adverse Event (AE)/Relationship to Study Drug, Device, and/or Procedure			Page 1 of 3	

1. PURPOSE

To provide guidelines to assess the causal relationship between an Investigational Product (IP) and an adverse event.

2. SCOPE

Applies to the Principal Investigator (PI), and when delegated by the PI, additional Investigator(s), Study Coordinators (SCs), and other designated site personnel.

3. RESPONSIBILITIES

The PI is responsible for assessing the relationship between the study drug, device, or procedure(s) and an adverse event.

4. BACKGROUND

Adverse events (AEs) are used by the PI and study personnel to monitor the safety of the drug, device, and/or procedure being studied. It is the PI's responsibility to determine the relationship between the AE and the study drug, device, or procedure. The following guidelines describe the subtle gradations between an AE, which is "likely" or "almost certainly" related to the study drug, and one that is "unlikely" or "clearly unrelated" to the study drug.

5. PROCEDURE

5.1. **Likely (almost certainly)** a causal relationship exists when the event:

- 5.1.1. is a well-known effect of the drug (listed in the PDR, investigator's brochure (IB), etc.) or device;
- 5.1.2. follows a clear temporal sequence from the drug's administration or device implantation/activation;
- 5.1.3. ceases with discontinuation of the drug or device (and reoccurs on restarting);
- 5.1.4. is clearly not related to study participant (SP) or study environment factors.

5.2. **Probably a causal** relationship exists when the event:

- 5.2.1. is a known or suspected effect of the drug or device (documented or not);
- 5.2.2. follows a reasonable temporal sequence from the drug's administration or device implantation;
- 5.2.3. ceases or diminishes with discontinuation of the drug or removal/discontinued activation of the device;
- 5.2.4. cannot be readily explained by the SP or study factors.

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- 5.3. **Possibly** a causal relationship exists when the event:
- 5.3.1. is a known or possible effect of the drug or device;
 - 5.3.2. follows a fair temporal sequence from the drug's administration or device implantation/activation;
 - 5.3.3. can be explained by the SP or study factors.
- 5.4. **Unlikely (remote)** that a causal relationship exists when the event:
- 5.4.1. is NOT a known or suspected effect of the test drug or device;
 - 5.4.2. is a possible or known effect of the drug or device;
 - 5.4.3. does NOT follow a temporal sequence from drug administration or device implantation/activation;
 - 5.4.4. can be readily explained by the SP or study factors.
- 5.5. **Unrelated** as a causal relationship exists when the event:
- 5.5.1. is NOT known to be an effect of the test drug or device;
 - 5.5.2. does NOT follow a temporal sequence from drug administration or device implantation/activation;
 - 5.5.3. can be readily and easily explained by the SP and study factors.

These guidelines are provided to assist in the medical decisions necessary to determine safety of a study drug, device, and/or procedure. It is the PI's responsibility to determine the relationship between a study drug, device, and/or procedure and an AE, based on best judgment, knowledge, and experience. Cases or study types presenting unusual or complicating factors may make the above thought process unusable. In these cases, the PI is expected to use his/her best judgment as to the causal relationship. In addition, some sponsors will have their own systems that may further enhance determination of the causal relationship for an AE.

6. TERMS & ABBREVIATIONS

AE	Adverse Events
IB	Investigator's Brochure
IP	Investigational Product
PDR	Physicians' Desk Reference
PI	Principal Investigator
SC	Study Coordinator
SP	Study Participant

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7. REFERENCES

7.1. ICH GCP Consolidated Guideline - Part 4.7 Randomization Procedures and Unblinding

8. ATTACHMENTS

None