Subject Injury	CR-108
Clinical Research Standard Practices	**Effective Date:** June 2024

SCOPE AND PURPOSE This document is applicable to the following roles within Penn State College of Medicine and Penn State Health entities engaged in clinical research:

Roles:

X	Principal Investigators	X	Regulatory Specialists
X	Sub-Investigators	X	Key Study Ancillary Personnel
X	Study Coordinators/Associates	X	Financial Analyst/Research Accountants
X	Data Specialists	X	Central Research Office Personnel

This policy describes how the term the "Subject Injury" shall be defined by Penn State College of Medicine and Penn State Health (collectively "the Institution") and what subject injury language shall be considered acceptable for for-profit sponsors.

It is the Institution's preference to use the term "participant" for individuals participating in a clinical research study which is not congruent with industry standard term of "Subject Injury." The interchangeability of the terms "participant" or "subject" outside of this policy does not alter applicability.

This policy may be shared externally upon request.

POLICY AND PROCEDURE STATEMENTS

1. The Institution shall define a Subject Injury as an adverse event, illness, or injury to a research participant that is determined to be related, probably related, or possibly related to the investigational product (the drug or device being evaluated in the study) in accordance with the study protocol or the proper performance of any procedure required by the protocol that would not have been performed but for the participant's involvement in the study.
    a. While expectedness of an event to the investigational product is a critical assessment for reporting to regulatory authorities, expectedness is not a consideration when determining if an adverse event, illness, or injury is a Subject Injury.
    b. The determination of relatedness is assessed by the Institution's local Principal Investigator or Sub-Investigator using the five-point scale: 1) not related, 2) unlikely related, 3) possibly related, 4) probably related, and 5) related. The definitions of these terms are defined in CR-304: Adverse Event Reporting
    c. The term "adverse event" above shall be read to be synonymous with Serious Adverse Event, as assessed by the Institution's local Principal Investigator or Sub-Investigator, with the event meeting one of the following criteria:
        i. Death

ii. Life-threatening, or suspected that the participant was at substantial risk of dying at the time of the adverse event or use or continued use of the investigational product might have resulted in the death of the patient.
iii. Hospitalization or prolongation of hospitalization was a result of the adverse event.
- Emergency room visits that do not result in admission to the hospital should be evaluated for one of the other serious outcomes (e.g., life-threatening; required intervention to prevent permanent impairment or damage; other serious medically important event).

iv. Disability or permanent damage, or risk of imminent disability or permanent damage if not for immediate intervention
- Substantial disruption of a person's ability to conduct normal life functions (i.e., significant, persistent, or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities and/or quality of life)

v. Congenital anomaly/birth defect
vi. Other serious important medical events
- An event may jeopardize the participant and may require medical or surgical intervention/treatment to prevent one of the other outcomes.

d. If a Sponsor or Clinical Research Organization (CRO) requires/requests that an event be "downgraded" from a Serious Adverse Event to an Adverse Event, it shall remain a Subject Injury.
e. Penn State University (PSU) and Penn State Health (PSH) have adopted the position that for-profit sponsors must accept responsibility for the payment for all complications and/or injuries sustained by research participants because of their participation in research. Because of this position, any adverse event, illness, or injury with a causation relationship of possibly related or greater shall be the Sponsor's responsibility.
    i. As Sponsor will only be responsible for procedure performed properly, any procedure not performed properly will not be classified as a Subject Injury but will still require appropriate reporting as an adverse event or serious adverse event and may require reporting to the IRB and regulatory authorities.

2. In clinical trial agreements, the first position should always be the PSU's standard subject injury language ("SIL"):

    Sponsor will provide reimbursement for the standard charges for the reasonable and necessary treatment required by the Study participant for any Study injury, adverse event, or illness caused by or derived from the administration of the Study Drug (or Study Device) or Study procedures performed under the agreed upon Protocol. Institution agrees to provide or arrange for prompt diagnosis and treatment of any Study injury, adverse event, or illness experienced by a Study subject as soon as Institution becomes aware of the Study injury, adverse event, or illness. Institution further agrees to promptly notify Sponsor of any Study injury, adverse event, or illness upon awareness.

3. If revisions are required by sponsor, please keep the following four points in mind as being non-negotiable:

a. Language referencing a for-profit sponsor charging the participant's insurance provider(s) for research-related injuries must be removed.
    i. When payments are made by sponsors of clinical trials for complications or injuries arising out of the trials, such payments by Sponsor are deemed to be liability insurance, including self-insurance.
    ii. A Sponsor's offer to pay research-related injuries in the CTA and ICF are considered payments by a liability insurance plan/policy, thus would invoke "Medicare Secondary Payer" status, requiring Sponsor to be primary payer.
b. Language that ties the cause of the research related injury "directly" to the use of the study drug or device. In these cases, the word directly must be deleted.
c. References to the participant not following instructions or being negligent must be removed or clarified to reference that the failure to follow instructions was intentional.
d. References to the injury, adverse event, or illness not being covered if it is attributable to the natural progression of an underlying or pre-existing condition or events, must include the clarifier "unless it's made worse by participating in the study."

4. If Sponsor refuses to agree to subject injury language on these terms, then the language may require approval by senior leadership, and should be sent to HRPP so that they can make any necessary changes to the Informed Consent Form.

5. Sponsor should agree to pay the "charge" of medical treatment rather than "cost." "Charge" is the standard amount PSH bills for a service regardless of who the responsible party is (i.e., medical insurance company, guarantor, or sponsor of a clinical research study). "Cost" is the actual cost of the service and does not include overhead or fees. Note: "expenses" instead of "cost" is also acceptable.
    a. Use of "cost" would require approval by senior leadership and application of overhead.

6. Template SIL for the ICF can be found in the *Consent Language Document* (HRP-109), though Sponsor's template language is acceptable if it conforms to the principles outlined in Sections 2 and 3 above.

RELATED POLICIES AND REFERENCES

Clinical Trials Office website (https://research.med.psu.edu/cto)

Medicare Guidance: Medicare, Medicaid, and SCHIP Extension Act of 2007, Section 111

Responsibilities of the Research Team (CR-103)

Site-Sponsor/CRP Communications (CR-210)
Adverse Event Reporting (CR-304**)**

Penn State University IRB: Consent Language Document (HRP-109)

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