



REPORTABLE EVENTS

New Information for Multi-site Studies that Requires Reporting to the USC IRB

Overview

Federal human research regulations require institutions to have written procedures to manage new information that requires prompt reporting to the IRB. Reporting to the USC IRB must be as soon as possible, but not later than 10 working days after the investigator becomes aware of the event.

The USC Overall PI/Lead Study team is responsible for submitting reportable events for all sites including USC to the USC IRB. The USC Overall PI/Lead Study will report events by completing a **Reportable Events** submission in iStar. Relying Sites will forward Reportable Events to the USC Overall PI/Lead Study team who will submit the report to the USC IRB via a **Reportable Events** submission in iStar. Relying Site should be prepared to provide input on corrective actions proposed by the USC IRB in connection with a reportable event.

When such new information is submitted for review, the IRB must determine whether the information represents:

1. An unanticipated problem involving risks to subjects or others;
2. Non-compliance with the federal regulations or with the requirements or determinations of the IRB; and
3. Non-compliance that is serious or continuing.

The USC IRB reviews research protocols to ensure there are adequate provisions for monitoring the data collected to ensure the safety of subjects. For studies involving more than minimal risk to subjects, a local USC monitoring plan is required. For research involving no more than minimal risks to subjects, the monitoring performed by the USC investigator is sufficient.

IRBs are not positioned to review individual events (data) except when events are unanticipated problems involving risk to subjects or others. IRBs need information to evaluate if the protocol risk to benefit ratio has changed, and whether criteria for approval continue to be met.

It is the responsibility of the study investigator to determine when internal or external adverse events, protocol deviations, incidents, or violations represent new information that requires prompt reporting of the information to the USC IRB. Investigators should also consider whether new information warrants changes to the protocol to minimize risks to subjects, and/or a change to the informed consent document to better inform subjects of the potential risks and the procedures needed to minimize such risks.

This guidance document provides definitions of the various types of research events, both medical and social behavioral examples of reportable new information to submit promptly to USC IRB.



This guidance document provides definitions and examples (both medical and social behavioral) of various types of research events considered reportable new information to be submitted promptly to USC IRB.

Definitions of Reportable Events

Adverse Event: Any untoward or unfavorable occurrence in a human subject (physical or psychological harm) temporally associated with the subject's participation in the research (whether or not related to participation in the research).

Adverse Reaction: Any adverse event caused by a drug. Adverse reactions are a subset of all suspected adverse reactions where there is reason to conclude that the drug caused the event. A suspected adverse reaction means any adverse event for which there is a reasonable possibility that the drug caused the adverse event. For the purposes of IND safety reporting, 'reasonable possibility' means there is evidence to suggest a causal relationship between the drug and the adverse event. A suspected adverse reaction implies a lesser degree of certainty about causality than an adverse reaction.

Deviation: Any intended or unintended variance or exception from the IRB approved protocol. This term, used interchangeably with the term "violation," is most often used when the variance is intended for the safety of one or more research participants, or an unintended change that is not considered as serious as a violation, and may involve no more than minimal risk to participants or others.

External Adverse Event or Outcome: An event or outcome that is experienced by subjects enrolled at study site(s) (e.g., multicenter clinical trial) under the jurisdiction of other IRBs.

Incident: An undesirable and unintended, although not necessarily unexpected, event or outcome involving any aspect of the research study.

Internal Adverse Event or Outcome: An event or outcome that is experienced by subjects enrolled at study site(s) under the jurisdiction of the Reviewing IRB (e.g., USC).

Noncompliance: Noncompliance is the failure to follow federal, state, local, or institutional regulations and policies governing human research or failure to comply with the determinations of the IRB. Noncompliance may involve any individual conducting research. Additionally, if any reasonable individual would foresee the event as compromising the rights and welfare of a subject or others, the noncompliance may be considered serious. If the noncompliance recurs after a report of the activity has been evaluated and corrective action has been mandated, noncompliance may be deemed to be continuing noncompliance.

Related (probably or possibly related): In the opinion of the USC investigator there is a reasonable possibility that the event, or outcome may have been caused by the procedures involved in the research.

Serious Adverse Event: Any adverse event that may result in the following: 1) death; 2) a life



threatening (places subject at immediate risk of death from the event as it occurred); 3) In-patient hospitalization or prolonged existing hospitalization; 4) a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; 5) congenital anomaly/birth defect. The occurrence of a serious adverse event suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized.

Unanticipated Problem: An unanticipated problem involving risks to subjects or others includes any incident, experience, or outcome that meets all of the following criteria:

- *unexpected* (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied
- *related or possibly related* to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research), and
- suggests that the research *places subjects or others at a greater risk of harm* (including physical, psychological, economic, or social harm) *than was previously known or recognized*

Unexpected: The nature, severity or frequency of the event or outcome is not accurately reflected in the protocol-related documents, such as the IRB approved research protocol, informed consent document, and investigator brochure; and/or the characteristics of the subject population being studied.

Unexpected Adverse Event: Any adverse event where the nature, severity or frequency of the event is not consistent with either: 1) the known or foreseeable risk associated with the procedures involved in the research that are described in the protocol-related documents (IRB approved protocol, informed consent document, investigator brochure), and relevant sources of information (product labeling/package inserts); or 2) the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.

Violation: Any intended or unintended variance, exception or deviation from the IRB approved protocol. This term, often used interchangeably with "deviation" is sometimes considered a more serious variance from an approved protocol than a deviation and is not normally used when the variance is made intentionally to eliminate an immediate hazard to one or more research participants.

Reportable New Information

It is the policy of the USC IRB that study investigators report new information (reportable events) if it falls into one or more of the categories below. Reportable new information must be submitted to the USC IRB as soon as possible and no later than **10 business days**. Information that does not fall under any of these categories does not require reporting to the IRB.



If the reportable event does not require a change to the research, it should be submitted alone. If the event requires an amendment (e.g., change in the study status, protocol revisions, consent form changes, etc.), submit an amendment concurrently with the reportable event. If an amendment is not ready for submission, describe what amendments are forthcoming.

1. Information that indicates a new or increased risk, or a new safety issue.

Examples:

- New information (e.g., an interim analysis, safety monitoring report, publication in the literature, sponsor report, or investigator finding) indicating an increase in the frequency or magnitude of a previously known risk or uncovers a new risk.
- Withdrawal, restriction, or modification of a marketed approval of a drug, device, or biologic used in a research protocol
- Protocol violation that harmed subjects or others or that indicates subjects or others might be at increased risk of harm
- Complaint of a subject that indicates subjects or others might be at increased risk of harm or at risk of a new harm
- Any changes significantly affecting the conduct of the research
- Unanticipated adverse device effect (any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device)

2. Harm experienced by a subject or other individual, which in the opinion of the investigator are unexpected and probably or possibly related to the research procedures.

- A harm is “unexpected” when the nature, severity, and frequency are inconsistent with risk information previously reviewed and approved by the IRB.
- A harm is “probably or possibly related” to the research procedures if in the opinion of the investigator, the research procedures more likely than not caused the harm.

3. Noncompliance with the federal, state, local, or institutional regulations and policies governing human research or failure to comply with the determinations of the IRB, or an allegation of such non-compliance

- Institutional audit or inspection of research
- Audit, inspection, or inquiry by a federal agency and any resulting reports (e.g., FDA Form 483.)
- Written reports of study monitors that identify non-compliance with the approved protocol
- Repeated failure to follow the protocol due to the action or inaction of the investigator or research staff that suggests non-compliance with the protocol
- Breach of confidentiality
- Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a subject
- Incarceration of a subject in a study not approved by the IRB to involve prisoners
- Complaint of a subject that cannot be resolved by the research team
- Premature suspension or termination of the protocol by the sponsor, investigator,



or institution

Reporting of Deviations/Violations and Incidents

Deviations/Violations should be reported to the IRB when protocol required procedures are accidentally or intentionally not met.

Examples of deviations/violations include, but are not limited to the following:

- Any unintended or intended deviation/violation from the IRB approved protocol.
- Use of expired or incorrect informed consent documents
- Enrollment of subjects not eligible according to the IRB approved protocol
- Any medication error involving dosing, administration and/or preparation of the study drug(s)
- Any lapse in study approval where there is a continuation of research activities (i.e., recruitment, enrollment, procedures, data analysis)

Examples of incidents include, but are not limited to the following:

- Any complaint of a study subject related to the research that cannot be resolved by the research staff
- Any breach of confidentiality
- Incarceration of a study subject in a medical study not approved to enroll prisoners
- Loss of adequate resources to support continued research activities
- An unexpected natural disaster, such as an earthquake, which destroys records or disrupts study scheduling
- Computer data security breach (e.g., lost or stolen computer/laptop and/or removable media used as storage devices, such as a flash drive or CD) in which personally identifiable information may have been acquired by an unauthorized person.

Note: This information will be reported to the USC Compliance Office by the USC IRB

IRB Responsible and Reviewing Procedures

The IRB is responsible for reviewing new information and determining if it meets the criteria of an unanticipated problem involving risk to subjects and others, and/or non-compliance. The IRB will reassess the risk to benefit ratio of the study, and whether the criteria for approval continue to be met. The IRB may require additional action from the investigator such as:

- Changes to the study protocol and consenting documents
- Procedures to inform subjects of new information that may affect their willingness to continue participation in the study
- Additional safeguards to protect the safety and welfare of subjects, including subject privacy and the confidentiality of data
- Changes to the corrective action plan to prevent the event or problem from recurring

IRB Reporting Requirements

Unanticipated problems involving risks to subjects or others; any serious or continuing noncompliance; and any suspension or termination of IRB approval are reportable to the USC institutional personnel and or committee, and appropriate federal department or agency head(s) as applicable.