Event Reporting
Human Subjects Research Procedures

I. Introduction

Federal regulations and TCU require prompt reporting to the IRB, appropriate institutional officials, sponsors (if any), and appropriate regulatory agency of certain events affecting participants in Human Subjects Research. These procedures supplement the Protections of Human Subjects in Research Policy (the "Policy") and outline these reporting requirements.

II. Definitions

All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

Adverse Event ("AE"). Any untoward or unfavorable sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the Human Subject's participation in the Research, whether or not considered related to the subject's participation in the Research, including any undesirable and unintended effect of research occurring in Human Subjects as a result of the collection of identifiable private information under the Research; and any problems associated with the use of an investigational device that adversely affects the rights, safety, or welfare of subjects. Medical condition/diseases present before starting the investigational drug/device/intervention will be considered AEs only if they worsen after starting study treatment/intervention.

Monitoring Entity. The group that is responsible for overseeing the safety of all subjects enrolled in the study in accordance with the protocol (e.g., a Data Safety Monitoring Board (DSMB), a Data Monitoring Committee (DMC), a coordinating or statistical center, or a sponsor).

Possibly related to the Research. There is a reasonable possibility that the AE, incident, experience, or outcome may have been caused by the procedures involved in the Research. This definition includes events that are definitely or probably related to the Research. To be unrelated to the Research, the cause of the AE is known and the event is in no way related to any aspect of Research (e.g. disease progression).

Protocol Deviation. Any change, divergence, or departure from the study design or procedures of a Research protocol that is under the investigator's control and that has not been approved by an IRB. Any change, divergence, or departure from the study design or procedures of a research protocol that affects a Human Subject's rights, safety, or wellbeing and/or the completeness, accuracy, and reliability of the study data constitutes a **protocol violation**. Changes or alterations in the conduct of the protocol that do not have a major impact on the subject's rights, safety, or well-being, or the completeness, accuracy and reliability of the study data are considered minor protocol deviations.

Serious AE. Any AE that meets any of the following criteria:

- Results in death;
- Is life-threatening (places the subject at immediate risk of death from the event as it occurred);
- Requires inpatient hospitalization or prolongation of existing hospitalization;
- Results in a persistent or significant disability/incapacity;

- Results in a congenital anomaly/birth defect; or
- Any other AE that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

Suspension. A temporary cessation of IRB approval includes a stop to the enrollment of new subjects, activities involving previously enrolled subjects and other research activities

Termination. A permanent cessation of IRB approval prior to study expiration that includes permanent halt in the enrollment of new subjects, approved activities involving previously enrolled subjects and other research activities

Unanticipated Problem. Any incident, experience, or outcome involving risks to the Human Subjects or others 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 a subject's participation in the Research; and
- Suggests that the Research places the Human Subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or recognized.

Unexpected AE. Any AE occurring in one or more Human Subjects in a Research protocol, the nature, severity, or frequency of which is not consistent with either:

- The known or foreseeable risk of AEs associated with the procedures involved in the Research that are described in (a) the protocol–related documents, such as the IRB-approved Research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or
- The expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the AE and the subject's predisposing risk factor profile for the AE.

Note: the majority of AEs occurring in Human Subjects are not Unanticipated Problems; a small proportion of AEs are Unanticipated Problems; and Unanticipated Problems include other incidents, experiences, and outcomes that are not AEs.

III. Reporting Requirements

A. Event Reporting. A PI, designee, or any other party with knowledge of any AEs, Protocol Deviations, or Unanticipated Problems must report such event to the TCU IRB within five working days upon discovery. Event Reporting requirements are in addition to, and do not supplant, any other required, periodic reports to the IRB.

1. AEs. When reporting an AE, the PI should consider the following details:
   - Was the event expected or unexpected?
   - Is the event a Serious AE?
   - What is the relationship of the AE to the Research participation? If there is any uncertainty regarding AE causality, then the event must be assessed as Possibly related to the Research and reported to the IRB as indicated.

2. Unanticipated Problems. Unanticipated Problems must be reported to the IRB regardless of whether they occur during the study, after study completion, or after participant withdrawal or completion. Such events also must be reported to appropriate entities under the applicable law.

3. Protocol Deviations. Below is a non-exclusive list of examples of protocol deviations. The severity of the deviation is determined by the IRB and resulting action depends on the specific circumstances of the deviation.
   - Failure to obtain informed consent or research authorization, i.e., there is no documentation of informed consent/research authorization or Informed consent/research authorization obtained after initiation of study procedures.
   - Informed consent/research authorization obtained by someone other than individuals authorized by IRB to obtain consent/research authorization, e.g., someone other than the PI or key personnel.
   - Inappropriate documentation of informed consent/research authorization.
   - Deviation that compromises the scientific integrity of the data collected for the study (e.g., subject was enrolled but does not meet the protocol's eligibility criteria; changing the protocol without prior IRB approval; inadvertent loss of samples or data).
   - Enrollment:
     - of a subject who did not meet all inclusion/exclusion criteria.
     - of subjects after IRB-approval of study expired.
     - of an ineligible subject.
     - over the number of subjects approved.
   - Failure to submit continuing review application to the IRB before study expiration.

- Use of invalid consent form, e.g., consent form without IRB approval, or outdated/expired consent form/research authorization.
- Omitting or failing to follow an approved portion of the protocol.
- Implementation of unapproved recruitment procedures except for the purpose of subject safety.
- Missing original signed and dated consent form/research authorization (only a photocopy available).
- Missing pages of executed consent form/research authorization.
- Copy not given to the person signing the form/research authorization.

B. When to Report. In all circumstances, the PI must report the event to the IRB promptly, using the IRB Event Reporting Form, which can be found on the IRB webpage. No event should be reported later than ten (10) working days from discovery. Below are specific reporting requirements, according to the type of event:

Unanticipated Problems: Notification of event is due to the IRB Chairperson within twenty-four (24) hours of learning of the event. Notification must be through either email or fax and must include a brief summary of event. Report is due to the IRB within five business days from notification to the IRB Chairperson.

Serious AE: Report is due to IRB within five (5) business days of learning of the event.

All AEs other than Serious AEs: Report is due to IRB within ten (10) business days of learning of the event.

Protocol Deviations/Violations: Report is due to IRB within ten (10) business days of learning of the event.

C. IRB Action.

1. Determination of Event Classification. The IRB Chairperson will review the event report within twenty-four (24) hours after receipt and determine if the event represents an Unanticipated Problem. Such determination will consider the following:

    - Was the event unexpected;
    - Does the event indicate 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;
    - Should the enrolled participants be informed of the Unanticipated Problem;
    - Does the protocol still satisfy the requirements of the IRB approval;

- Should the informed consent be revised; and
- Other corrective action.

If the IRB Chairperson believes that immediate action is needed to ensure the safety of the Research subjects, the Chairperson may request that the investigator suspend all research procedures pending IRB further review at a convened meeting. If the PI refuses to voluntarily suspend Research activity, the IRB Chairperson may take action to formally suspend the Research study through the IRB.

2. Notifications.

   a. If the IRB Chairperson determines that the event is not an Unanticipated Problem, the event is managed according to its classification and severity, as determined by the IRB Chairperson. Minor Protocol Deviations and most AEs are managed exclusively by the IRB. Majority Protocol Deviations/violations, and Severe AEs are managed by the IRB, in coordination with the Institutional Official ("IO"), unless otherwise referred the Research Integrity Officer ("RIO"). If the event is managed by the IRB, the IRB may take any action within their authority deemed appropriate by the IRB, up to and including suspension or termination of a Research study. If the event is referred to the RIO, no further action is taken under these policy and procedures. Instead, the Research Integrity policy and procedures apply. Once adequately addressed to the IRB's satisfaction, the matter is closed and no further action is necessary.

   b. If the IRB Chairperson determines that the event is an Unanticipated Problem:

      i. The Chairperson must place the matter on the agenda for the next scheduled IRB meeting.

      ii. All IRB members shall be given a copy of the event report, the IRB-approved protocol and documents associated with protocol.

      iii. As with all full board reviews, a primary reviewer will be designated by the Chairperson (the Chairperson may designate themselves). The primary reviewer is provided any previous reports of unanticipated problems involving risks to subjects or others related to the protocol.

      iv. The convened IRB considers the following actions:

         - No action
         - Modification to the protocol or other study documents
         - Modification of the information disclosed during the consent process
         - Require additional information for current or past subjects
         - Re-consent of current subjects taking part in the study
         - Modification of the continuing review schedule
         - Suspension of the study

- Termination of the study
- Refer the matter to other internal parties (e.g. IO, RIO, legal counsel)
- Other action appropriate for the circumstances

v. Notify the IO.

D. Institutional Official Action. The Institutional Official or designee, with assistance from the IRB Chairperson, will report the institution's determination and findings to all appropriate TCU officers and to relevant regulatory agencies.

IV. Related Research Policies and Procedures

Research Integrity Policy
Research Integrity Procedures
Policy for the Protection of Human Subjects
Human Subjects Research Procedures
Human Subjects Research Oversight and Monitoring Policy
Human Subjects Research Oversight and Monitoring Procedures

V. Effective Date

Effective Date: January 21, 2019