IRB SOP 601
Unanticipated Problems and Adverse Event Reporting

Purpose

The purpose of this standard operating procedure (SOP) is to ensure that adverse and serious adverse events are defined, recorded, reported, and evaluated as required by the USA Institutional Review Board (IRB).

Scope

This SOP applies to all research involving human subjects that is conducted at USA or any of its affiliate institutions. Application of this SOP starts at the time the subject signs the initial Informed Consent Form and continues through 30 days after the subject completes the active part of the study, unless otherwise stated.

Policy

Investigators are responsible for prompt reporting to the IRB of "any unanticipated problems involving risks to participants or others..." (45CFR46.103.b (5)). The IRB maintains responsibility for initial assessment of the risk/ benefit ratio in a research activity involving human participants. During the course of the project, investigators are required to promptly inform the IRB of any unanticipated negative effect or undesirable experience that is possibly, probably or definitely related to study procedure(s).

Adverse events are not necessarily physical in nature; attention must be paid to psychological harm (such as depression, thoughts of suicide, etc.), threats to privacy, or participant safety. An event is considered serious and must be reported when the participant experiences an unusually strong response, recurring problems, and/or death.

Definitions

Adverse Event: The University's policies on adverse events are based on Food and Drug Administration regulations. According to the FDA, a "**serious** adverse drug experience" with respect to human clinical experience includes "any experience that suggests a significant

g. significant overdose or protocol error; or
h. certain medical events that may not result in death, be life-threatening, or require hospitalization, may also be considered a serious adverse event when appropriate medical or surgical intervention is necessary to prevent one of the outcomes listed above.

Observational Studies: Submission of adverse events on observational studies, which is research on materials collected for non-research purposes: These studies do not involve intervention from the study physician, and the subject only provides authorization for the usec450 Td ref[illegible]EMBT

Updates or follow-up reports are not required unless the non-serious event becomes a serious adverse event or unless otherwise stated by the Board. If this upgrade in severity occurs then procedures in section 3.0 should be followed.

3.0 Serious Adverse Event Reporting

All serious adverse events that are unexpectedly associated with the study procedures must be reported to the sponsor and the IRB immediately, but no later than 7 working days upon learning of the event using the USA Adverse Event Report Form.

Serious adverse events, unless otherwise stated in this policy, should be reported from the time of informed consent through 30 days after the end of study participation.

Serious Adverse Event Reporting	
TYPE OF EVENT	**Report to IRB**
Serious AND unexpected AND related, possibly related, or probably related	5 working days

Updates or follow-up reports are not required unless the serious adverse event ends with a death or unless otherwise stated by the Board. If this upgrade in severity occurs than procedures in section 3.1 should be followed.

3.1 Death

Deaths judged to be the result of progressive cancer disease do not need to be reported. All other deaths, whether or not they are directly related to study procedures, must be reported. Deaths must be submitted to the IRB within three working days from the time the first member of the study team is aware of the event.

Deaths must be reported throughout the subject's participation on a study including the active and follow-up period.

Death Reporting	
TYPE OF EVENT	**Report to IRB**
Death	3 working days

4.0 Unanticipated Problems

Unanticipated problems in a study which might affect subject risk benefit analysis, confidentiality, or subjects' willingness to continue in a project are to be reported to the IRB.

The IRB will consider the effect of the problem on the study and on the subjects already enrolled.

In some instances, revisiting the consent process with previously enrolled subjects may be necessary. If the problem prompts a change in the study, the consent process and documentation may require alteration for future study subjects. The investigator should use his/her own judgment when determining if an event is considered reportable beyond the scope of this policy.

Examples of unanticipated problems include:

- An accidental or unintentional change to the IRB approved protocol that placed one or more participants at increased risk, or has the potential to occur again.
- A change to the protocol made without prior IRB review to eliminate an apparent immediate hazard to a research participant.
- Interim findings and/or a safety monitoring report that indicate an unexpected change to the risks or potential benefits of the research in terms of severity or frequency.
- Publication in the literature that indicates an unexpected change to the risks or potential benefits of the research.
- A complaint of a participant that indicates unexpected risks or that cannot be resolved by the research team.
- Incarceration of a participant in the course of a study.
- A change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
- A breach of a participant's confidentiality or privacy that involves potential risk to that participant or others.

Unanticipated Problem Reporting	
TYPE OF EVENT	**Report to IRB**
Unanticipated Problem	7 working days

5.0 IRB responsibilities following receipt of SAE/Follow-up Report

The Adverse Events designated member of the IRB reviews all adverse event reports and/or incident reports in order to re-evaluate the risks/benefits of the study and/or the appropriateness of the recruitment/consent process to determine if any changes should be made in the protocol or consent form. If the investigator has already modified the protocol or consent form in response to these events, the appropriateness of these changes is also reviewed. The Adverse Events reviewer may recommend additional review by the full IRB. The IRB office will provide acknowledgement of receipt of this information and request additional

information if follow-up or clarification is needed. The full committee has the right to request additional information from the investigator, note the occurrence of the adverse event but take no action, ask the investigator to modify the protocol or the informed consent or suspend or terminate the project.

The IRB is responsible for continuing review of all human subject research. This is done through the annual renewal process required for any ongoing study. Thus, all reported adverse events should also be described in detail in the Annual Renewal Report Form when a renewal application is submitted for the study, so that the IRB may consider renewal of the protocol in light of such information.

5.0 Safety Alerts, IND Safety Reports, MED Watch Reports

During the course of a study, IND Safety Reports or other adverse event reports are provided from the sponsor. The IRB does not require submission of these reports. The reported information will be inserted into an updated investigator's brochure. The investigator's responsibility is to ensure that the risk/benefit relationship of the research remains acceptable.

Related Federal Regulations

45 CFR 46.130(b)(5); 21 CFR 56.108(b); 21 CFR 812.3(s)

Related Guidelines

FDA – Adverse Event Reporting to IRBs – Improving Human Subject Protection

OHRP "Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks & Adverse Events Guidance, 2007

HISTORY

Effective Date:
Revisions: October, 2018