8.3 Review of Unanticipated Problems Involving Risk to the Subject or Others

1.0 Purpose

The purpose of this policy is to describe the process for reporting potential unanticipated problems (UPs) involving risk to the ORA and the IRB, and the process for review of potential UPs.

2.0 Policy

It is the policy of the organization that:

- 2.1. The ORA and the IRB will comply with HHS regulations at 45 CFR 46.108(a)(4)(i); any additional requirements of Common Rule agencies (as applicable); and FDA regulations at 21 CFR 56.108(b)(1), 21 CFR 312.32(a), and 21 CFR 812.3(s) (as applicable).
- 2.2. Any AE, UADE, noncompliance event, complaint, or other incident, regardless of the level of associated or potential risk, which appears to meet the criteria for classification as a UP will be submitted to the full IRB for review.
- 2.3. The convened IRB is responsible for determining whether the event, incident, outcome, or complaint meets the criteria for classification as a UP.

3.0 Definitions

- 3.1. Unanticipated Problems Involving Risk to Subjects or Others (UP) is defined as an event that meets the criteria below:
  - 3.1.1. The event is unexpected in terms of specificity, severity, or frequency, considering the nature of the research, the characteristics of the subject population, and the information contained in the protocol, protocol-related documents, and the ICF. In addition, the event is not consistent with the expected natural progression of any underlying disease, disorder, or condition of the subject.
  - 3.1.2. The event is related, or possibly related to subjects' participation in the research or procedures involved in the research. This means there is a reasonable possibility that the event may have been caused by procedures involved in the research or resulted from participation in the research by the subject.
  - 3.1.3. The subject or others suffered harm, or were placed at greater risk of harm (including physical, psychological, economic, social, or legal) than was previously known or recognized when the IRB approved the research either initially, at continuing review, or at the time of approval of a Request for Change.
  - 3.1.4. Though not a required criterion for definition of an event as a UP, the event generally warrants substantive changes in the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects or others.

  Note: A UP may arise from an AE, UADE, noncompliance, complaint, or other incident (including new information such as IND safety reports, DSMB reports, or other outcome information).
  Note: UPs may occur in research other than clinical trials, and may involve risks other than physical harm (for example, a stolen laptop or thumb drive containing identifiable information leading to risk of loss of confidentiality).

4.0 Investigator (or Other Reporters') Responsibilities

- 4.1. Reports of AEs/UADEs are submitted in accordance with HRPP policy 8.1 (IRB Review of Adverse Events and Adverse Device Effects).
- 4.2. Reports of complaints are submitted in accordance with HRPP policy 8.2 (IRB Review of Study Related Complaints).
- 4.3. Reports of noncompliance are submitted in accordance with HRPP policy 8.4 (Review of Noncompliance Involving the PI and Study Personnel).
- 4.4. IND safety reports, DSMB reports, or other outcome information on risk are submitted in accordance with HRPP policy 3.2 (Data and Safety Monitoring).
- 4.5. Reports of other unanticipated events related to the research that either expose subjects or others to potential risk or result in harm, but do not fall under the reporting requirements above must be promptly reported to the IRB as an Incident Report thru RSS.

5.0 IRB/ORA Responsibilities

- 5.1. The ORA will review reports under Section 4.1 thru 4.5 above in accordance with the criteria specified in HRPP policies 2.2 (Full IRB Review), HRPP policies 8.1 (IRB Review of Adverse Events and Adverse Device Effects), HRPP policies 8.2 (IRB Review of Study Related Complaints), and HRPP policies 8.4 (Review of Noncompliance Involving the PI and Study Personnel), and will make determinations (including referral to the convened IRB) as described in those policies.
- 5.2. Events reviewed by the ORA in accordance with the above policies will be referred to the convened IRB if a determination is made by the ORA that the event may constitute a UP.
- 5.3. The convened IRB will determine whether or not the event is a UP in accordance with Section 3.1 of this policy.
- 5.4. The IRB will ensure all necessary steps will be taken in order to protect the rights and welfare of human subjects and maintain compliance with applicable federal regulations and HRPP policies.
- 5.5. In addition to the required actions specified in HRPP policy 2.2 (Full IRB Review), IRB actions may include, but are not limited to:
  - 5.5.1. Requiring modification of the protocol.
  - 5.5.2. Requiring modification of the information disclosed during the consent process.
  - 5.5.3. Requiring notification of current participants when such information might relate to participants' willingness to continue to take part in the research.
  - 5.5.4. Requiring provision of additional information to past participants.
  - 5.5.5. Requiring current participants to re-consent to participation.
  - 5.5.6. Modification of the continuing review schedule.
  - 5.5.7. Monitoring of the research.
  - 5.5.8. Monitoring of the consent process.
  - 5.5.9. Referral to other organizational entities.

6.0 Reporting UPs to Institutional Officials, OHRP, FDA, and Department or Agency Heads

All required reports will be submitted in accordance with HRPP policy 8.7 (Reporting Incidents to Institutional Officials and Federal Agencies).

DOCUMENT HISTORY:

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Revised: 1/18/2023 - Clarified that certain events are always referred to convened IRB for review and determination if the event constitutes a UP, and other events are first reviewed by the ORA and only referred if determined by the ORA to be potentially represent a UP; simplified text; stylistic changes. {Approved Rusty McCulloh (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

Revised: 5/8/2023 - Corrected regulatory reference in section 2.1; modified section 5.1 to reflect IRB actions as opposed to investigator actions (eg, "requiring modification of the protocol" as opposed to "modifying protocol"); correcting misspellings.{Approved Rusty McCulloh (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

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