

## **EVENT REPORTING – UNANTICIPATED PROBLEMS INVOLVING RISKS TO SUBJECTS OR OTHERS, ADVERSE EVENTS, AND OTHER PROBLEMS**

### **1.1. Overview**

Federal regulations require the University to have written procedures for insuring that unanticipated problems involving risks to subjects or others are promptly reported to the IRBs, appropriate institutional officials, and federal agencies. The IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Unanticipated problems can occur in any type of research (medical or non-medical) and may include occurrences such as adverse events, research participant complaints, protocol deviations, and other untoward events involving risk. Events requiring prompt reporting by Investigators and research staff may involve physical, psychological, social, legal, or economic harms.

### **1.2. Definitions**

**Unanticipated problems involving risks to subjects or others:** Unforeseen events (given the nature of the research procedures and subject population) that suggest participants, research staff, or others are placed at greater risk by the research than previously expected. Unanticipated problems involving risks to subjects or others may be medical or non-medical in nature, and include – but are not limited to – *serious, unexpected, and related adverse drug events* and *unanticipated adverse device effects* (see below).

**Adverse event (AE):** Any undesirable and unintended (although not necessarily unexpected) effect occurring as a result of interventions, interactions, or collection of identifiable private information in research. In medical research, any untoward physical or psychological occurrence in research, including abnormal laboratory finding, symptom, or disease temporally associated with the use of (although not necessarily related to) a medical treatment or procedure. Adverse events involving drugs are also referred to as *adverse drug experiences*.

**Serious adverse event (SAE):** An adverse event that is fatal or life threatening, permanently disabling, requires or prolongs hospitalization, or results in significant disability, congenital anomaly, or birth defect.

**Unexpected adverse event:** An adverse event that has not been previously observed or is not consistent in nature, severity, or frequency with existing risk information, such as in the investigator brochure, research protocol, consent form, or other available information (e.g., IND application for an investigational drug).

**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, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application; any other unanticipated, serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

**Related:** Associated or having a timely relationship with; a reasonable possibility exists that an outcome may have been caused or influenced by the event in question (e.g., administration of a study drug), although an alternative cause/influence may also be present. Related events may be *definitely*, *probably*, or *possibly* related.

**Unrelated:** Unassociated or without a timely relationship; evidence exists that an outcome is definitely related to a cause other than the event in question.

**Internal event:** An event occurring in research at OSU or at a site(s) under an OSU IRB's jurisdiction.

**External event:** An event occurring in research at a site(s) other than OSU, over which another (non-OSU) IRB has jurisdiction.

### 1.3. Events Requiring Prompt Reporting

Investigators and research staff are responsible for reporting to the IRB unanticipated problems involving risks to subjects or others. The convened IRBs are responsible for making the final determination that a reported event (e.g., adverse event) is an unanticipated problem involving risks to subjects or others.

The following events may represent unanticipated problems involving risks to subjects or others and should be promptly reported:

- Adverse events or injuries that are serious, unexpected, and related;
- Adverse device effects that are unanticipated;
- Protocol deviations or violations (or other accidental or unintentional changes to the protocol or procedures) involving risks or with the potential to recur;
- Events requiring prompt reporting according to the protocol or sponsor;
- Complaints made by research participants indicating an unanticipated risks, or complaints that cannot be resolved by the research staff;
- Unapproved changes made to the research to eliminate an apparent immediate hazard to a research participant;
- Data and Safety Monitoring Board (DSMB) reports, interim analyses, or other oversight committee/monitoring reports altering the risk/benefit profile;
- New information indicating an unexpected change in risks or potential benefits (e.g., literature/scientific reports or other published findings);

- Investigator's Brochure (IB or IDB) updates or revisions to safety information; and
- Other problem or finding (e.g., breach of confidentiality, loss of study data or forms, etc.) that an Investigator or research staff member believes could influence the safe conduct of the research.

Both internal (generally on-site) and external (generally off-site) events as defined above should be promptly reported.

#### **1.4. Timeframe for Reporting**

The events described above should be reported to the IRB using the [Event Reporting Form](#) **within 10 days** of the Investigator's or research staff member's learning of the event. **Events resulting in temporary or permanent interruption of study activities by the Investigator or sponsor to avoid potential harm to participants should be reported immediately (within 48 hours) whenever possible.**

All internal and external events that may represent unanticipated problems involving risks to subjects or others should be promptly reported (as above), regardless of whether they occur during or after the study, or to a subject who has withdrawn from or completed study participation. If changes to the research or consent process are proposed as a result of the event, or if additional information will be provided to current and/or past participants, an [amendment request](#) must also be submitted for IRB review.

#### **1.5. Events Not Requiring Prompt Reporting**

Potential risks and adverse events that may be reasonably anticipated (i.e., "expected") should be described in the informed consent process/form and do not require prompt reporting to the IRB by Investigators and research staff. The following are examples of events that do not require prompt reporting:

- Adverse events or injuries that are non-serious, expected, or unrelated;
- Adverse device effects that are non-serious, anticipated, or unrelated;
- Deaths not attributed to the research, e.g., from "natural causes," accidents, or underlying disease and the Investigator has ruled out any connection between the study procedures and the participant's death;
- Protocol deviations or violations not involving risks to participants or unlikely to recur;
- Complaints made by research participants not involving risks or complaints that were resolved;
- DSMB reports, interim analyses, or other reports, findings, or new information not altering the risk/benefit profile;
- IB updates not involving safety information; and

- Problems or findings not involving risk (unless the Investigator or research staff member believes the information could affect participants' willingness to continue in the research).

Related internal and external events involving risk, but not meeting the prompt reporting requirements, should be reported to the IRB in summary form at the time of [continuing review](#). A current DSMB report can be submitted for research subject to oversight by a Data and Safety Monitoring Board (or other monitoring entity), in lieu of a summary of external events. External events that do not meet the reporting requirements and that are not relevant to the protection of participants in research at OSU or at a site(s) under an OSU IRB's jurisdiction need not be reported. Investigators should retain copies of all individual event reports on file.

For a flowchart of event reporting requirements, see Figure 1.

## **1.6. Review Process**

Event reports and accompanying information will be screened for completeness by ORRP IRB Protocol Analysts, who will make an initial determination about whether the event represents a possible unanticipated problem involving risks to subjects or others. These events will be forwarded to the convened IRB for review. Reports of events that do not meet the requirements for prompt reporting may be returned. All other event reports will be reviewed by the expedited procedure.

### **1.6.1. Expedited Review**

Event reports and accompanying information will be forwarded by ORRP IRB Protocol Analysts to the appropriate IRB Chairperson, Vice-Chair, or one of the experienced members with relevant expertise designated by the Chair for expedited review. Reviewers will be provided the complete protocol file, including previously reported events, for review. The Chairperson or designee will determine if the report raises new concerns about risks and will recommend further review by the convened IRB, as necessary, for a final determination. The IRB Chair or Vice-Chair may suspend or terminate approval of an Investigator's research if necessary to assure the protection of research participants. The Chair or Vice-Chair will consider the rights and welfare of participants when suspending, terminating, or modifying research.

If during expedited review the event is determined not to be an unanticipated problem involving risks to subjects or others, the reviewer will make any necessary recommendations for action (see below), which will be communicated to the Principal Investigator by ORRP. Modifications proposed by the Investigator or IRB reviewer that represent minor changes will also be reviewed by the expedited

procedure. IRB members will be informed of these expedited reviews in the monthly summary of all other reviews performed by the expedited procedure.

### **1.6.2. Convened Review**

Reports of events determined by ORRP screening or expedited IRB review to represent possible unanticipated problems involving risks to subjects or others will be forwarded to the IRB for convened review. Modifications proposed by the Investigator or IRB reviewer that represent more than minor changes will also be reviewed by the convened IRB. The Chair, Vice-Chair, or other member with relevant expertise will serve as the primary reviewer. Copies of the reports, all other information provided by the Investigator, and current consent documents (or verbal scripts) with any proposed changes will be included in the review materials for each IRB member. Sections from the protocol, previous event reports, and other relevant information or reference materials will also be included, as applicable. The complete protocol file will be available to any IRB member upon request prior to or during the convened IRB meeting.

By convened review the IRB will determine whether the event is an unanticipated problem involving risks to subjects or others and if further action is necessary. Action(s) will be based on the nature of the event, degree to which research participants are placed at risk, occurrence of previous problems, etc. The IRB will consider the rights and welfare of participants when suspending, terminating, or modifying research.

### **1.6.3. IRB Actions**

The types of actions that the IRB may consider for any event include, but are not limited to:

- Modification(s) of the research protocol or procedures;
- Modification(s) of the consent process or consent form;
- Additional information should be provided to current research participants (required when such information may relate to their willingness to continue in the research);
- Additional information should be provided to past research participants;
- Current research participants should be re-consented;
- Additional follow-up/monitoring is required for current and/or past research participants;
- Monitoring of the research (including audits) or consent process;
- Education or mentoring for the Principal Investigator and/or research staff;
- Additional reporting is required, including modification of the continuing review schedule;

- Additional resources are needed to support the Investigator’s research activities;
- Limitations (e.g., restriction to co-investigator status) on the Investigator’s research activities;
- Suspension or termination of the research; and
- Referral to other appropriate University process (e.g., misconduct review).

The IRB’s determination and action(s), including votes taken, will be recorded in the meeting minutes. The requirements for quorum and majority apply. Investigators will be notified in writing by ORRP of IRB decisions regarding events determined not to represent unanticipated problems involving risks to subjects or others following approval of the meeting minutes by the IRB Chair or Vice-Chair. Suspended IRB approval may be reinstated, as appropriate, based on the outcome of the convened review. Investigators (and others) will be notified of IRB actions regarding events determined to be unanticipated problems involving risks to subjects or others as described below.

### **1.7. Institutional Reporting**

If the IRB determines that an event is an unanticipated problem involving risks to subjects or others, or if the Board suspends or terminates approval of research that is associated with unexpected serious harm to subjects, the Investigator(s), IRB, Institutional Official, and the Investigator(s)’ Dean and Department Chair (or equivalent) will be notified of the reasons for the IRB’s action in writing by ORRP within 14 days of the determination. OHRP, FDA (as applicable for FDA-regulated research), the sponsor or any other sponsoring federal Department or Agency, and others (e.g., Sponsored Programs) as necessary, in accordance with The Ohio State University’s Federalwide Assurance, will be notified in writing within 30 days. The content of the report will conform to OHRP requirements for incident reporting.

### **1.8. Record Retention**

Records of reports and reviews of events representing possible unanticipated problems involving risks to subjects or others, including submission materials and communications, are retained by ORRP for at least three years, in keeping federal regulation, applicable state and local law, and University policy.

### **1.9. Applicable Regulations/Guidance**

21 CFR 50.25(b)(5), 21 CFR 56.108(b)(1), 21 CFR 812.150(a)(1), 45 CFR 46.103(b)(5)(iii), 45 CFR 46.116(b)(5), OHRP “Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events” (01/15/07), OHRP “Guidance on Reporting Incidents to OHRP” (05/27/05)

**Figure 1.**

**Flowchart for Reporting Events to the IRB**

