GUIDELINE FOR REPORTING RESEARCH EVENTS

OHSP Policy 801 defines the requirement for the Investigator to determine whether an event or problem must be reported to the RSRB or another non-UR Reviewing IRB (i.e., a reportable event). This guideline outlines the procedures for determining whether a research event or problem is reportable, the timeframe for reporting depending on the characteristics of the event, how to report to RSRB, as well as the procedures the RSRB will follow to report applicable events to institutional and regulatory authorities. When considering whether an event needs to be reported to a non-UR Reviewing IRB, the Investigator should follow guidelines from the Reviewing IRB.

1. Investigator Review and Assessment of Event

   a) Investigators and research staff are responsible for assessing whether a research incident, experience, or outcome such as those listed below is an unanticipated problem involving risks to subjects or others.
      - Adverse event or injury from drug, device or non-medical procedure or activity.
      - Breaches of confidentiality.
      - Data and Safety Monitoring Board (DSMB) reports, interim analyses, or other oversight committee/monitoring reports altering the risk/benefit profile.
      - Investigator’s brochure updates/revisions to safety information (excluding routine updates).
      - New information indicating an unanticipated change in risks or potential benefits (e.g., literature/scientific reports or other published findings).
      - Protocol deviations, violations, or other changes (intentional or otherwise) to the protocol or procedures involving risks or with the potential to recur.
      - Subject complaints or complaints that cannot be resolved by the research staff.
         - Note: Researchers must also take into account any additional departmental policies and procedures when resolving any complaints or concerns arising from the conduct of research.
      - Changes made to the research to eliminate an apparent immediate hazard to a subject(s).
      - Other problem or finding (e.g., loss of study data or forms, a subject becomes a prisoner while participating in research, etc.).
      - Other events that may prompt reporting requirements according to the protocol, sponsor, or funding agency.

   b) If the Investigator becomes aware of any of the events noted above and determines that the event is considered unanticipated, related, and serious, or involves increased risks to subjects or others than was previously known or expected, or meets both of these definitions, the event must be reported to the RSRB (see Appendix 1 Research Event Reporting Flow Chart). Both internal and external events involving subjects participating in research under the University of Rochester’s Human Subject Protection Program should be given this assessment.
2. **Timeframe for Reporting to RSRB**

a) If the Investigator determines that an event requires reporting, it should be reported to the RSRB using the ‘Reportable Event’ form in the RSRB On-line Submission System (ROSS) **within 10 calendar days** of the Investigator’s or research staff member’s learning of the event. All internal and external events should be promptly reported, regardless of whether they occur during or after the study, or involve a subject who has withdrawn from or completed study participation.

When a problem occurs in a study reviewed and approved by a central IRB (e.g., Western IRB), the event is reported directly to the central IRB. Additional investigation of the event may be conducted by the RSRB as necessary; however, as necessary, any required external reporting will be conducted by the RSRB Director.

*Examples of External Reportable Events:*
- “Dear Investigator” letter notifying the site of a trend based upon adverse events reported in the entire study.
- Data Safety Monitoring reports that require an action to the study (e.g., terminate the study, terminating an arm of the study, adding risks to the consent form, etc.).
- Annual Manufacturer HUD Reports.

b) The event should be reported as one of the following categories. For a detailed description and examples of each category, see the Guideline to RSRB Categories of Reportable Events.

- Type 1 – Serious Adverse Events
- Type 4 – Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO)
- Type 5 – Monitoring Reports
- Type 6 – New Information
- Type 7 – Changes Without Approval
- Type 8 – Non-Compliance
- Type 9 – Voluntary Suspension

i. When submitting a Reportable Event, rather than using the automated title “Reportable Event #1 for RSRBXXXX”, change to further clarify what is being submitted, for example:
- DSMB report dated XX/XX/XXXX
- UPIRTSO – Laptop computer stolen on XX/XX/XXXX”

ii. The report must include a description of the event, the date of occurrence, the type of harm or risk, whether the event was internal or external, unanticipated, the outcome, and an assessment of degree of relatedness to the research. The report should also include effect on subjects and/or others, as applicable, and any corrective and preventive action plan the Investigator has implemented.

*Note:* If there are any proposed changes to protocol materials being initiated (including change in consent documents or other notification procedures) see 2d below.
c) Events resulting in temporary or permanent interruption of study activities by the Investigator or sponsor to avoid potential harm to subjects should be reported within 48 hours of awareness of the event whenever possible.

d) At the time of reporting, 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 subjects, complete an Amendment request along with the Reportable Event form. The Amendment will be reviewed according to the amendment review procedures outlined in Policy 502 Types of RSRB Submissions.

3. Events Not Requiring Prompt Reporting to RSRB

a) If a local event is NOT deemed unanticipated, and serious, and related, or it does not additionally involve increased risks to subjects or others, do not report until the time of continuing review. In Section 5 of the ROSS Continuing Review application, report these as a summary of events with an assessment of risk (e.g., no change, greater/less than expected, etc.). Non-local events are submitted to the RSRB only if they represent an increased risk to the subjects who are participating locally (i.e., event requires a change in the protocol or consent form).

b) For external events that have no effect on the risks to subjects participating at University of Rochester (and affiliates), do not submit to the RSRB as the report will not be reviewed.

Examples of external, non-reportable events:
- Manufacturer IND safety reports.
- Reports of individual Serious Adverse Events (SAEs) that took place at other sites (i.e., sites not under the responsibility of the UR Investigator or the RSRB).

4. RSRB Review Process

Event reports and accompanying information will be forwarded to the appropriate RSRB Chair to determine whether the report meets the criteria as a reportable event, or may be sent directly to be reviewed at the time of the next continuing review, as applicable. If the Chair determines the report is not considered a reportable event, this will be documented within ROSS and the report will be sent back to the study team for revision. If the information is appropriately reported, the Chair may then make a determination as to whether the reportable event may be given an expedited review or that it requires review by the convened board (see below).

a) Expedited Review of Reportable Event
The Chair, or designated primary reviewer, will have access to the complete protocol file, including previously reported events, for review. The Chair or designee will determine if the report raises new concerns about risks and will recommend further review by the convened RSRB, as necessary, for a final determination. The Chair or designee may suspend or terminate approval of an Investigator’s research if necessary to assure the protection of research participants. The Chair or designee will consider the rights and welfare of subjects 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 (UPIRTSO), the reviewer will make any necessary recommendations for action or request for more information (see section 5 below), which will be communicated to the Investigator by the RSRB Specialist. A determination requiring no further action will be documented in ROSS and the Investigator is notified of this outcome. Reports that were reviewed by expedited procedures will be reported to the convened board.

b) **Convened RSRB Review of Reportable Event**

Reports of events determined to meet the reporting requirements upon initial receipt, or during initial review by the Chair, will be forwarded for convened board review. The Chair, or other member with relevant expertise, will serve as the primary reviewer. Copies of the report(s) and all other relevant information will be included in the review materials for each RSRB 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 is available within ROSS to any RSRB member prior to or during the convened RSRB meeting.

The RSRB will determine by convened review whether the event meets the criteria of a reportable event, and if so, whether it is an unanticipated problem involving risks to subjects or others. In either case, the RSRB will also determine if any further action is necessary. Action(s) will be based on the nature of the event, degree to which research subjects are placed at risk, occurrence of previous problems, etc. The RSRB will consider the rights and welfare of subjects when suspending, terminating, or modifying research.

### 5. RSRB Review Determination

The range of possible actions that the RSRB may consider for any reported event include, but are not limited to the following, all of which will be communicated to the Investigator:

- No action
- Modification of the protocol
- Modification of the information disclosed during the consent process
- Providing additional information to former subjects
- Notification of current subjects when such information may relate to subjects’ willingness to continue to take part in the research
- Requirement that current subjects re-consent to participation
- Modification of the continuing review schedule
- Monitoring of the research
- Monitoring of the consent process
- Suspension of the research approval
- Termination of the research approval
- Referral to other organizational entities (e.g., OHSP, University Audit, UR Office of Counsel)
- Corrective and Preventative Action plan (CAPA) to explain what has been done to correct the event or occurrence, as well as a plan to prevent such an event from occurring again.
The RSRB’s determination and action(s), including any votes taken, will be recorded in the meeting minutes. The requirements for quorum and majority vote apply. Suspended RSRB approval may be reinstated, as appropriate, based on the outcome of the convened review. Investigators (and others) will be notified of RSRB actions regarding events determined to be unanticipated problems involving risks to subjects or others as described below.

6. **Institutional and Regulatory Reporting**

If the RSRB 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, notification to the Investigator, institutional officials, regulatory authorities, and others will be completed as required following the Guideline for RSRB Institutional and Regulatory Reporting of Suspension, Termination and Non-Compliance.

NOTE: Investigators conducting human gene transfer research must submit a written report of serious adverse experiences that are unexpected and associated with the use of the gene transfer product to the NIH Office of Biotechnology Activities (NIH/OBA), the UR Institutional Biosafety Committee, the RSRB, and the FDA or study sponsor within specified timeframes as found in Appendix M-I-C-4 in the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines). Gene transfer investigators must submit annual reports to OBA as set forth in Appendix M-I-C-3 of the NIH Guidelines.
Appendix 1 – Research Event Reporting Flow Chart

Does the Investigator assess the event as Unanticipated?
• An experience that wasn’t expected or not consistent with existing risk information (e.g., protocol, consent, IB)

Yes

Does the Investigator assess the event as Related to the research?
• Event that is directly associated with or caused by some aspect of the subject’s participation in the study (e.g., research procedure, laptop database); “Related” = definitely, probably, or possibly related

Yes

No

Does the Investigator assess the event as Serious AND/OR potentially places subjects or others at an increased risk of harm (UPIRTSO) such as physical, psychological or social?
• Serious = Fatal or life threatening, permanently disabling, requires or prolongs hospitalization, or results in significant disability, congenital anomaly, or birth defect; causes a prolonged or permanent harm that is psychological, social, legal, or financial.
• Examples of increased risk or harm to others = breach of confidentiality, investigational drug dosing error, publication of ‘anonymous’ results in a defined population.

Yes – Serious only

Yes – UPIRTSO only

Yes – Serious and UPIRTSO

No

Complete Reportable Event Type 1 and submit within 10 calendar days

Complete Reportable Event Type 4 and submit within 10 calendar days

Complete Reportable Event Type 4 and submit within 10 calendar days

Summary report at the time of continuing review

Does the RSRB determine the event is unanticipated, serious and related?

Yes

No

Does the RSRB determine the event is a UPIRTSO?

Yes

No

Notification to Investigator with any additional action requested (e.g., CAPA, consent change)

Notification to Investigator and additional reporting to OHRP, FDA, Sponsor, etc. as required

Notification to Investigator with any additional action requested (e.g., CAPA, consent change)

Do not submit external events that have no effect on risks to subjects at UR.