

**SYRACUSE UNIVERSITY  
HUMAN RESEARCH PROTECTION PROGRAM  
STANDARD OPERATING PROCEDURES**

<b>TITLE: REPORTING OF UNANTICIPATED PROBLEMS INVOLVING RISK TO PARTICIPANTS OR OTHERS</b>		<b>DOCUMENT NUMBER: 027</b>	
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**Title: REPORTING OF UNANTICIPATED PROBLEMS INVOLVING RISK TO PARTICIPANTS OR OTHERS**

**1.0 Purpose:**

The purpose of this Standard Operating Procedure (SOP) is to outline the process for reporting unanticipated problems involving risk to participants or others.

**2.0 Policy:**

It is the policy of the Syracuse University (SU) Institutional Review Board (IRB) to require reporting of unexpected harms or unanticipated problems involving risk to participants or others.

- 2.1** The following requires reporting to the SU IRB within 10 working days of the Investigator's knowledge of the problem:
  - 2.1.1** Any event that in the Investigator's opinion was unanticipated, involved risk to participants or others and was possibly related to the research procedures;
  - 2.1.2** Any event that requires prompt reporting to the sponsor in accordance with the protocol;
  - 2.1.3** Any accidental or unintentional change to the IRB-approved protocol that increases risk or decreases benefit, affects the participant's rights, safety, welfare, or affects the integrity of the resultant data;
  - 2.1.4** Any accidental or unintentional change to the IRB-approved protocol that has the potential to recur;
  - 2.1.5** Any deviation from the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research participant;
  - 2.1.6** Any publication in the literature, safety monitoring report including a Data and Safety Monitoring Report, interim result, or other finding that increases risk or decreases benefit, affects the participant's rights, safety, welfare, or affects the integrity of the resultant data;
  - 2.1.7** Any event that is both a serious event and an unexpected event, which in the Investigator's opinion is more likely than not to be related to the research procedures;
  - 2.1.8** A breach in confidentiality that may involve risk to that individual or others;
  - 2.1.9** Any complaint of a participant that indicates an unanticipated risk or which cannot be resolved by the research staff; and
  - 2.1.10** Any other event that, in the opinion of the Investigator, constitutes an unanticipated risk.
- 2.2** Any unanticipated problem listed above requires reporting to the IRB even after the participant has completed the study or after the participant has withdrawn from the study until study closure.
- 2.3** A summary of all harms associated with the study and any independent safety monitoring reports or Data Safety Monitoring Board reports must be reported to the SU IRB at the time of continuing review as an assessment of the risk profile of the research. Individual reports are not required (See *SOP 015*).

### **3.0 References and Reference Documents:**

45 CFR 46.103(b)(5)

*SOP 015, IRB Continuing Review*

*SOP 029, Suspension or Termination of IRB approval*

*Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events*, Office for Human Research Protections (OHRP), January 15, 2007

*SOP 030, Reporting to the Appropriate Institutional Officials, and the Department or Agency Heads*

### **4.0 Procedure:**

#### **4.1 Investigator Responsibilities.**

**4.1.1** The Investigator submits any event that requires reporting according to this policy and any other event that may represent an unanticipated problem involving risk to participants or others as follows:

**4.1.1.1** A “Report of Unanticipated Problem Involving Risk to Participants or Others” Form is submitted to the IRB as soon as possible, but no later than 10 working days after the Investigator first learns of the event or problem. This form contains the Investigator’s assessment of causality (related or not related to the study) and a description of the actual event;

**4.1.1.2** Any associated materials such as medical record notations or reports with the name and medical record number of the individual redacted (removed); and

**4.1.1.3** When applicable, a “Request for Amendment” Form indicating changes associated with the event or problem is submitted.

**4.1.2** The Investigator is responsible for the accurate documentation, investigation, and follow-up of all unanticipated problems involving risk to participants or others that occur at the site in which the Investigator is responsible for the conduct of the research.

#### **4.2 IRB Chair/Designated IRB Member Responsibilities.**

**4.2.1** All reports made under the policy are provided to the IRB Chair or a designated IRB Member for review within 2 working days.

**4.2.2** The reviewer is provided:

**4.2.2.1** A copy of the report and all attachments; and

**4.2.2.2** The IRB file.

**4.2.3** The IRB Chair reviews the materials to determine whether the risk-potential benefit profile has changed.

**4.2.4** The IRB Chair reviews the materials to determine whether the event represents an unanticipated problem involving risk to participants or others as follows:

**4.2.4.1** The IRB Chair evaluates whether the event meets the following criteria:

**4.2.4.1.1** Unanticipated (i.e., the event was not foreseeable) 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;

**4.2.4.1.2** related or possibly related to participation in the research (*possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

**4.2.4.1.3** suggests 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.

**4.2.5** If the IRB Chair cannot make a determination for each criterion, the event will be forwarded to the full IRB to make these decisions. The Chair can not decide a problem requires no further action without determining that the problem is not an unanticipated problem involving risks to participants or others.

- 4.2.6 If the IRB Chair determines that the event meets all criteria, then the event will be considered an unanticipated problem involving risk to participants or others and the event will be referred to the IRB for further action. If participants are at immediate risk of harm and there is insufficient time to wait for review by the convened IRB, the IRB Chair or designated IRB Member may immediately institute an “Administrative Hold” according to *SOP 029*.
- 4.2.7 If the IRB Chair determines that the event does not meet all criteria, then the event will be considered not to represent an unanticipated problem involving risk to participants or others, the report will be accepted and signed by the IRB Chair. However, if the event alters the IRB approved protocol, proposal, informed consent document or risk-potential benefit profile, then most likely the problem (1) was unanticipated and (2) caused harm or increased risk of harm to participants or others and the event will be forwarded to the full IRB to make a decision about whether the event was an unanticipated problem involving risks to participants or others.

### 4.3 IRB Responsibilities.

- 4.3.1 Each unanticipated problem involving risks to participants or others is reviewed by the convened IRB.
- 4.3.2 If the IRB Chair could not determine whether the reported event represented an unanticipated problem involving risks to participants or others, the convened IRB will determine whether the event meets the following criteria:
  - 4.3.2.1 Unanticipated (i.e., the event was not foreseeable) 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;
  - 4.3.2.2 related or possibly related to participation in the research (*possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
  - 4.3.2.3 suggests 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.
- 4.3.3 The IRB may postpone a decision while awaiting additional information. In such cases, the IRB will consider the appropriateness of an “Administrative Hold” on the research until a final determination is made.
- 4.3.4 If the IRB determines that the event meets all criteria, then the event will be considered an unanticipated problem involving risk to participants or others and the following actions may take place:
  - 4.3.4.1 The IRB will consider the following actions:
    - 4.3.4.1.1 Accept the report with no changes;
    - 4.3.4.1.2 Accept the report with changes to the risk-potential benefit ratio, the protocol, or the informed consent documents;
    - 4.3.4.1.3 Request re-consenting of participants or require notification to participants (including past participants) of the changes. The changes to the consent or the notification document must be approved by the IRB prior to notification;
    - 4.3.4.1.4 Request further information from the Investigator;
    - 4.3.4.1.5 Increase the frequency of continuing review;
    - 4.3.4.1.6 Impose additional monitoring;
    - 4.3.4.1.7 Place the study on “Administrative Hold” pending receipt of further information;
    - 4.3.4.1.8 Suspend the study according to IRB Policy on Suspension or Termination of IRB Approval with:
      - 4.3.4.1.8.1 Suspension of recruitment;

- 4.3.4.1.8.2 Suspension of screening and enrollment;
- 4.3.4.1.8.3 Suspension of intervention and interaction; or
- 4.3.4.1.8.4 Suspension of follow-up.
- 4.3.4.1.9 Terminate the study for Cause according to IRB Policy on Suspension or Termination of IRB Approval (see *SOP 029*).
- 4.3.4.2 The event will be reported according to IRB Policy on Reporting to the Appropriate Institutional Officials, and the Department or Agency Heads (see *SOP 030*).
- 4.3.4.3 The IRB will consider whether the event represents serious or continuing non-compliance according to IRB Policy on Investigating and Managing Potential Issues of Non-Compliance (*SOP 028*).
- 4.3.4.4 In the case of deviations from the protocol taken without prior IRB review to eliminate apparent immediate hazard to a research participant, the IRB will consider whether the changes were consistent with the rights and welfare of participants.
- 4.3.5 If the IRB determines that the event does not meet all criteria, then the event will be considered not to represent an unanticipated problem involving risks to participants or others, and the report may be accepted by the full IRB and signed by the IRB Chair or designee with no further action.

#### 4.4 ORIP Responsibilities.

- 4.4.1 Upon receipt of a “Report of Unanticipated Problems Involving Risk to Participants or Others,” the ORIP Director facilitates review by the IRB Chair or designated IRB Member within 2 working days.
- 4.4.2 The ORIP Director will consult with the IRB Chair or designated IRB Member for assistance in determining the appropriate level of review for the “Report of Unanticipated Problems Involving Risk to Participants or Others.”
- 4.4.3 Events reported on the “Report of Unanticipated Problems Involving Risk to Participants or Others” Form that do not change the risk-potential benefit profile, study protocol or informed consent documents are signed by the IRB Chair or designated IRB Member.
- 4.4.4 Unanticipated problems involving risk to participants or others that change the risk-potential benefit profile, study protocol or informed consent documents are prepared for full IRB review. The ORIP/IRB Administrator places the items on the next IRB agenda, assigns Reviewers, and prepares Reviewer and IRB member packets. Reviewer packets for all IRB Members include:
  - 4.4.4.1 The “Report of Unanticipated Problem Involving Risk to Participants or Others”;
  - 4.4.4.2 The verbal report, if applicable;
  - 4.4.4.3 A safety report, if applicable;
  - 4.4.4.4 Any attached supplemental material submitted with the report;
  - 4.4.4.5 An amendment request, if applicable;
  - 4.4.4.6 The current IRB approved application and informed consent document;
  - 4.4.4.7 The sponsor’s protocol;
  - 4.4.4.8 Any other pertinent materials such as advertisements, questionnaires, etc.
  - 4.4.4.9 Any pertinent communications between the IRB staff and the investigator;
  - 4.4.4.10 Copies of pertinent section of the IRB file; and
  - 4.4.4.11 The complete IRB file will be available for review.
- 4.4.5 Final determination letters are drafted using the appropriate template.
- 4.4.6 Appropriate database entries are completed (i.e *InfoEd*).

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Approved by:

BR Ware

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Institutional Official

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7-20-08

Date

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Chair of the Institutional Review Board

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