Division of RESEARCH Research Compliance

Institutional Review Board (IRB) Procedures for Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events

1. **PURPOSE**
   1.1. The purpose of this policy is to describe the procedures the IRB office follows when:
      a. Determining if an incident is an adverse event (AE) directly related to the participation in a research study;
      b. Responding to an unanticipated problem that was not identified in the IRB protocol;
      c. Determining if an incident is reportable under Title 45 Code of Federal Regulations Part 46 (45 CFR 46), Protection of Human Subjects and Clemson University (CU) policies.

2. **SCOPE**
   2.1. This policy applies to all human subjects research under the oversight of Clemson University (CU) IRB, including cooperative research projects, regardless of the level of review of the study or the study status.

3. **POLICY STATEMENT**
   3.1. CU applies the federal regulations 45 CFR 46 when research is sponsored or overseen by a federal agency. When studies do not receive funding from, or are not otherwise regulated by, a federal agency, CU has adopted policies and procedures to accommodate difference in types of research. In these instances, CU adopted equivalent protections for participants.
   3.2. Researchers must promptly report the following incidents to the IRB office:
      a. An unanticipated problem or AE involving direct harm to participants.
      b. An unanticipated problem or AE related to the research that exposes participants to potential risk but that does not involve direct harm to participants.
      c. An unanticipated problem or AE related to the research that exposes individuals other than the research participants (e.g., investigators, research assistants, students, the public, etc.) to harm or potential risks.
      d. Information that indicates a change to the risks or potential benefits of the research. For example: An interim analysis or safety monitoring report indicates that frequency or magnitude of harms or benefits may be different than initially proposed in the IRB application.
      e. A paper is published from another study that shows the risks or potential benefits of the research may be different than initially proposed in the IRB application.
      f. A breach of confidentiality.
      g. Incarceration of a participant during a research study and the study was not approved to enroll prisoners.
      h. Change to the study protocol taken without prior IRB office review to eliminate an apparent immediate hazard to a research participant.
      i. Complaint by a participant when the complaint indicates unexpected risks or cannot be resolved by the research team.
      j. Protocol violation (meaning an accidental or unintentional change to the IRB approved protocol) that harmed participants or others or that indicates participants or others may be at increased risk of harm.
      k. Sponsor imposed suspension for risk.
      l. Any other incident that indicates participants or others might be at risk of serious and/or unanticipated harms related to the research study.

4. **REPORTING INCIDENTS TO THE IRB OFFICE**

4.1. Researchers must report the incidents to IRB office within the following timelines:

a. Researchers must report incidents requiring immediate intervention to prevent serious harm to participants or others within five (5) business days of receiving notice of the incident(s).

b. Researchers must report all other incidents no later than ten (10) business days of receiving notice of the incident(s).

4.2. Incidents occurring within thirty (30) days after participants complete the research activities or treatment must be reported according to the timelines in 4.1.

4.3. Researchers may report incidents to the IRB office:

a. By submitting the Reportable Incidents eForm through the IRB online submission system;

b. Notifying the IRB office by e-mail at IRB@clemson.edu or phone;

c. Contacting the ethics/safety hotline, https://www.clemson.edu/administration/internalaudit/ethicsline.html.

4.4. Initial Review of Reportable Incidents Report

a. The IRB Program Administrator will review the initial report to determine if additional information or documentation is required.

b. The IRB Program Administrator will notify the Principal Investigator (PI) that an incident was reported to the IRB office if the report was not submitted through the IRB online submission system or if the PI is not the individual reporting the incident. The name of the individual reporting the incident will not be shared with the PI if the person requests for their identity to remain confidential.

c. The IRB Program Administrator will notify the IRB Chair and Office of Research Compliance (ORC) Director of the incident to determine if immediate action is required to prevent additional harms or risks to participants or others.

5. **REVIEWING THE REPORTABLE INCIDENTS REPORT**

5.1. The IRB Program Administrator, ORC Director, and IRB Chair will review the report to determine if the incident is considered an adverse event and/or unanticipated problem.

a. The PI will be required to provide a written response if the incident was not submitted through the IRB online submission system or reported by the PI.

b. If the IRB Chair or designated IRB member will consider if either:

1. The incident was foreseen; OR
2. No participants or others were harmed; AND
3. Participants or others are not at increased risk of harm.

c. The IRB Chair or designee will document if the incident is an adverse event and/or unanticipated problem and what actions, if any, are required to ensure protection of the rights and welfare of participants and others.

d. If the IRB Chair or designee determines the incident(s) was “foreseen” and:

1. No participant(s) or others were harmed, the determination will be documented in the IRB record and the IRB Program Administrator will send a written response of the findings to the PI.
2. Participant(s) or others were not seriously harmed, the determination will be documented in the IRB record and the IRB Program Administrator will send a written response of the findings to the PI.
3. Participant(s) or others were seriously harmed, the IRB Program Administrator will schedule a convened meeting for the IRB members to review the Reportable Incidents Report and determine

what actions are required to ensure protection of the rights and welfare of participants and others.

e. If the IRB Chair or designee determines the incident(s) were "unforeseen" and:
   1. No participant(s) or others were harmed, the determination will be documented in the IRB record and the IRB Program Administrator will send a written response of the findings to the PI.
   2. Participant(s) or others were not seriously harmed, the determination will be documented in the IRB record and the IRB Program Administrator will send a written response of the findings to the PI.
   3. Participant(s) or others were seriously harmed, the IRB Program Administrator will schedule a convened meeting for the IRB members to review the Reportable Incidents Report and determine what actions are required to ensure protection of the rights and welfare of participants and others.

f. A report of incidents reviewed and determined not to impose increased risks of harm is periodically provided to the convened IRB and the Office of Research Compliance (ORC) Director.

6. CONVENED IRB REVIEW OF REPORTABLE INCIDENTS REPORT

6.1. The convened IRB reviews the incident report and IRB Chair or designee findings to determine if:

a. Further investigation is warranted;
b. The research protocol still satisfies the requirements for IRB approval under 45 CFR 46.111;
c. The identified risks to participants and others may be minimized and reasonable in relation to the anticipated benefits, if any, to the participants and others and the importance of the knowledge that may reasonably be expected to result;
d. The study procedures require modifications;
e. The continuing review or progress report timeline should be changed;
f. Additional IRB office monitoring of research activities is warranted;
g. Additional information about the study risks needs to be shared with current and previous participants and others;
h. The study staff needs additional training;
i. The study should be suspended or terminated;
j. Other actions are required to protect the rights and welfare of participants and others.

7. DETERMINATION AND FINDINGS

a. The IRB Program Administrator will send a written response of the findings to the PI, ORC Director, Department Chair, the college Associate Dean of Research (ADR), and other institutions IRB office for cooperative research projects.
b. If the IRB Chair, designee, or convened IRB determines that a report does represent an adverse event or unanticipated problem involving risks to subjects or others, the determination is reported to appropriate institutional officials, federal regulatory agencies (e.g., OHRP, FDA), research sponsors and others pursuant to the CU policies.

8. SANCTIONS

8.1. Individuals found to be in violation of this policy may be subject to sanctions relating to their participation in research with human subjects, up to and including permanent suspension or debarment from engaging in research with human subjects at CU.

8.2. Additional sanctions may be placed by federal regulatory agencies and research sponsors.

9. **CONFIDENTIALY**

9.1. The IRB members and IRB staff will follow all CU confidentiality policies during the review process, including protecting the identify of individuals reporting incidents to the IRB office.

10. **RETALIATION**

10.1. The ORC will assist with protecting individuals reporting incidents from retaliatory actions.

11. **ADDITIONAL RELATED RESOURCES**

a. CU:
   1. Division of Research policies, https://www.clemson.edu/research/division-of-research/research-policies.html
b. Research Misconduct Policy, https://www.clemson.edu/research/compliance/research-misconduct/
c. Whistleblower and Non-Retaliation Policy, https://www.clemson.edu/research/division-of-research/resources/policies.html
d. IRB Review Procedures and Other Policies, https://www.clemson.edu/research/division-of-research/offices/orc/irb/resources/index.html
e. U.S. Department of Health and Human Services (HHS) Office for Human Research Protections (OHRP) Guidance and Policies, https://www.hhs.gov/ohrp/regulations-and-policy/index.html

12. **RESPONSIBLE DEPARTMENT/DIVISION:**

12.1. The CU IRB Program Administrator should be contacted regarding questions or issues with this policy.

13. **PUBLISHED LOCATION:** This policy may be accessed on the IRB webpage, https://www.clemson.edu/research/compliance/irb/.

14. **APPROVAL & REVISION HISTORY**

14.1. Last Date of Revision: 6/2023

15. **REFERENCES**

15.1. Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events: OHRP Guidance (2007)

15.2. Title 45 Code of Federal Regulations Part 46 (45 CFR 46), Protection of Human Subjects

15.3. Policy adapted, with permission, from the Indiana University Human Research Protection Program (HRPP)