108 Adverse Events, Unanticipated Problems, and Non-Compliance	
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Policy

This policy describes how adverse events, unanticipated problems, and noncompliance related to the use of human subjects in research are handled in compliance with federal regulations, state law, and other institutional policies. As part of its responsibility to oversee the protection of research participants, the Institutional Review Board (IRB) investigates all complaints of adverse events, unanticipated events, or noncompliance, hereinafter referred to collectively as "Incidents."

Definitions

Incidents:

Adverse Events: Any untoward or unfavorable occurrence in a human subject, including both physical and psychological harm, contemporaneously associated with participation in the research, whether or not considered related to the subject's participation in the research activities.

Unanticipated Problem: Any accident, experience, or outcome that meet all of the following criteria:

1. 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;
2. Related or possibly (within reason) related to participation in the research; and
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.

Note: Incarceration of a participant while participating in a study that is not approved to include incarcerated individuals is considered an unanticipated problem.

Noncompliance: Failure (intentional or unintentional) to comply with applicable federal regulations, state or local laws, the requirements or determinations of the IRB, or university

policy regarding research involving human subjects. Noncompliance can result from action or omission. Noncompliance may be serious or non-serious (minor), and may also be continuing.

Non-serious or minor noncompliance: Noncompliance that does not increase risk to research participants, compromise participant's rights or welfare, or affect the integrity of the research/data or the Human Research Protection Program (HRPP). Minor noncompliances include, but are not limited to, lapses in continuing IRB approval, minor changes or deviations from an approved protocol, administrative errors, failing to add trained personnel to an approved protocol. Exceeding the approved number of participants by less than 10% of the total is considered a minor noncompliance. Failure to obtain exempt determination before exempt research is conducted will initially be reviewed as a minor noncompliance but may be escalated to serious noncompliance depending on the circumstances.
Serious noncompliance: Noncompliance that increases the risk to research participants, compromises participants' rights or welfare, or affects the integrity of the research/data or the HRPP. Examples include, but are not limited to, conducting or continuing non-exempt human subjects research without IRB approval, failure to follow approved IRB protocol, lack of legally effective informed consent from research participants, failure to report or review serious adverse events, unanticipated problems, or substantive changes in research; or inappropriate oversight of the study. Noncompliance related to the use of subject pools is considered serious.

Continuing noncompliance: Includes noncompliance that has been previously reported, or a pattern of may affect participants or research validity and suggest personnel may repeat noncompliance in the future. Examples include, but are not limited to, repeated failure to submit renewal requests, inadequate oversight of research personnel or procedures, or failure to respond to previous sanctions imposed by the IRB. Continuing noncompliance may be considered serious noncompliance by the IRB depending on the circumstance.

IRB noncompliance: means any failure on the part of the IRB to follow federal regulations, state laws or institutional policies relevant to human participants research.

Incident Reporting

1. Study teams must notify the Illinois State University IRB promptly of any potential Incident occurring in their research. Reports from the study team are made via the Incident Submission Form in Cayuse IRB.

    a. For purposes of this policy, promptly means study teams must report a potential Incident to the reviewing IRB within:

i. One (1) business day of receiving notice of the problem when immediate intervention is required to prevent serious harm to participants or others.

ii. Fourteen (14) business days from the date the study team is notified of the problem for all other potential Incidents.

2. For collaborative research, potential Incidents involving risks to participants or others occurring at a non-ISU research site must be reported to the ISU IRB if a) the potential Incident poses risks to ISU participants or b) the ISU IRB is serving as the reviewing IRB for the site at which the potential Incident occurred.

3. Potential Incidents can also be reported by other individuals not involved with the research project, but who have relevant information, including but not limited to IRB members or staff; participants or potential participants and their family members; members of staff of another IRB; REC staff or other University personnel.

   a. The report can be made to the Director of Research Ethics and Compliance (REC or designee) by phone or email and may be made anonymously. Reports may also be made through the University Ethics Office Complaint system. Reports will be handled in accordance with the University Whistleblower protections.

   b. For reports made to REC, the reporter will be asked to provide the following information:

      i. Detailed information about the potential Incident, including relevant dates.

      ii. How the person reporting obtained the information provided in the report.

      iii. Information about any injury, potential harm, or risk to the participant or others.

      iv. How the reporter may be contacted for further information, if needed.

      v. Any other relevant information requested by the REC Office.

4. Potential Incidents may also be encountered in the course of administrative review (review of a protocol, a grant proposal/compliance protocol congruence review, audit, etc.). Upon discovery or upon receipt of a report of a potential Incident from someone other than the investigator or

study staff, the Director of REC will notify the principal investigator (PI) on the study when appropriate.

Investigation

1. Reports of potential Incidents are initially evaluated by the Director of REC or designee to determine whether the problem likely constitutes an Incident. The Director may:
    - Interview the PI and co-investigators, selected human subjects, and others;
    - Examine research records requested from the investigators; and
    - May personally inspect research facilities and equipment.

    The Director may also consult with the General Counsel and the Institutional Official (IO) as necessary. Individuals with potential conflicts of interest shall not participate in the investigation.

    a. If the REC Director determines that a reported problem may require immediate intervention to protect participants or others from serious harm, the Director will immediately forward the report to the IRB chair (or designee).

    b. The REC Director has the authority, in consultation with the IRB Chair as necessary, to address minor noncompliance matters administratively. The Director may require modifications to the approved protocol, further documentation of the circumstances leading to the minor noncompliance, or other action as appropriate. The Director also has the authority to bring continuing minor noncompliance to the IRB for consideration.

    c. If the REC Director determines that the report constitutes a potential Incident that is not minor, the REC Director will refer the report to the IRB Chair (or designee).

        i. After reviewing the report, the IRB Chair (or designee) will determine whether further consultation is needed to assess whether the problem posed risks to participants or others.

2. If the IRB chair (or designee) determines that the report (i) does not constitute an Incident or (ii) does not require any action and that the research may continue without change, the IRB chair (or designee) will promptly notify the study team in writing when appropriate.

    a. If a report suggests that participant safety is at risk, the IRB chair may immediately suspend the protocol temporarily, pending IRB review.

b. The IRB Chair (or designee) may consult with other IRB members if special expertise is needed to assess whether the problem posed risks to participants or others.

c. Any report that appears to constitute a non-minor potential Incident will be referred to the convened IRB for review at the next available IRB meeting for review.

   i. If a report did not come from the study team, IRB staff may provide the study team with an opportunity to respond to the report before forwarding it to the IRB.

   ii. When appropriate, the IRB Chair (or designee) may make recommendations to the convened IRB as to what actions should be taken in response to the report.

IRB Review

1. The IRB will review reports of potential Incidents referred to it by the IRB chair (or designee). At any point in this process the IRB may invite the study team to present additional information.

   a. All IRB Members will be given access to the complete protocol file, including the Incident report, in Cayuse IRB.

   b. If a report suggests that participant safety is at risk, the IRB may immediately suspend or terminate the research.

   c. After considering the report and additional information, if any, the convened IRB will make final determinations on the following issues:

      i. Whether the reported problem constitutes an Incident involving risks to participants or others according to the definition in this policy

      ii. What action in response to the report is appropriate

      iii. Whether suspension or termination of approval is warranted, and

      iv. Whether further reporting to university officials, federal agencies and department heads is required.

d. Regardless of whether the IRB determines that the problem is an Incident involving risks to participants or others, according to the definition in the policy, and beyond the actions that may be undertaken by other bodies, the IRB may take any of the following actions:

   i. Modifying the consent document and/or process

   ii. Monitoring of the research and/or consent process

   iii. No action

   iv. Other actions appropriate for the local context

   v. Providing additional information to past and/or current participants (e.g. whenever the information may relate to the participant's willingness to continue participation)

   vi. Reconsidering approval

   vii. Referral to other organizational entities (e.g., legal counsel, risk management, institutional official)

   viii. Requirement that current participants re-consent to participation

   ix. Requiring additional training of the investigator and/or study staff

   x. Requiring modifications to the protocol

   xi. Revising the continuing review timetable

   xii. Suspending the research

   xiii. Terminating the research

   xiv. Disallowing the use of data collected without IRB approval

e. After making its determinations, the IRB will:

   i. Notify the investigator in writing of its decisions.

ii. If the IRB determines the problem constituted an Incident, it may notify any of the following individuals, institutions or organizations:

1. the chair of the investigator's department and/or unit

2. other administrative officials as relevant, such as the dean and/or division head, Director of Research and Sponsored Programs, and Institutional Official

3. Deferring institution if the continuing or serious noncompliance involves or may affect that institution's investigator(s) or participants

4. Other campus entities, such as the Data Stewardship Council, Protection of Minors Committee, and the Research Integrity Officer

5. Any other individuals, institutions, or organizations as appropriate

2. When the IRB suspends approval for a research project, research involving human subjects must be halted until and unless the IRB lifts the suspension. The PI must submit to the IRB modifications to the protocol sufficient to satisfy the conditions of the suspension and the modifications must be approved by the IRB before the research can be resumed. When the IRB terminates a research project no further research involving human subjects under the project may be undertaken. This includes analysis of data collected under the study. Any further research would require the submission and approval of a new study.

3. Suspension or termination of IRB approval can result in the freezing of internal or extramural grant accounts, the return of equipment or other resources, and further investigation by other entities. Flagrant or repeated violation of IRB policies and procedures is a violation of the University's Integrity in Research, Scholarly and Creative Activities policy. If the investigation contains facts that suggest research misconduct, the Research Integrity Officer must be notified.

4. Appeals may be submitted in writing to the REC Director and must be based on new information that was not previously available or considered by the IRB during the meeting at which the determination was made. The IRB will notify the PI in writing of the final determination.