

# Policy on IRB Review of Noncompliance

## Background

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Researchers are responsible for ensuring that their human subjects research activities are conducted in accordance with the protocol approved by the Iowa State University Institutional Review Board (IRB) and with applicable institutional policies and federal regulatory requirements. Failure to do so constitutes noncompliance.

Noncompliance ranges from minor administrative oversights to serious issues that jeopardize the safety, rights, and welfare of research participants. It may be an isolated incident or an ongoing problem.

Noncompliance can have widespread adverse outcomes. It jeopardizes public trust in research and places the Iowa State at risk of federal sanctions, up to and including losing federal funding for human subjects research. Therefore, it is imperative that Iowa State researchers take seriously their obligations to remain in compliance with IRB-related requirements. Researchers must also promptly report to the IRB any noncompliance of which they become aware.

The Vice President for Research (VPR), who serves as Iowa State's Institutional Official (IO) has designated the Iowa State IRB and staff in the Office of Research Ethics (ORE) as the responsible entities for:

1. investigating cases of potential noncompliance in human subjects research for which Iowa State serves as reviewing IRB;
2. reviewing cases and determining whether each is serious and/or continuing noncompliance;
3. recommending corrective actions for consideration by the IO;
4. external reporting, in accordance with federal requirements.

This policy describes the process by which incidents of noncompliance in human subjects research are handled at Iowa State.

## Scope

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This policy is applicable to human subjects research under the oversight of the Iowa State IRB.

## Definitions

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**Principal investigator (PI):** The individual ultimately responsible for the conduct of human subjects research, including oversight of investigators serving on a research team. Each IRB application must identify an individual as Principal Investigator. In cases where a Supervising Investigator is named per the policy on PI eligibility (e.g., student projects), the term "PI" also includes the individual listed as Supervising Investigator.

**Protocol or approved protocol:** The information included in the approved IRB application, including any attachments, addenda, or appendices. Information approved in subsequent amendments (e.g., modification, continuing review, closure) or status check submissions are included in this definition.

**Exempted protocol:** The information included in the final IRB application upon which a determination of exemption was granted, including any attachments, addenda or appendices, and subsequent amendments for modification or status check submissions.

**Noncompliance:** Any action or activity associated with the conduct or oversight of human subjects research that fails to comply with either the IRB-approved research plan, or federal regulations or institutional policies governing human subject research. Noncompliance can result from action or omission, and may be *minor*, *serious*, and/or *continuing* as defined below.

In general, intentional deviations from the approved protocol constitute noncompliance, unless enacted to eliminate apparent immediate hazards or risks to research subjects.

Unintentional or unavoidable deviations that are outside of the reasonable control of the researcher(s) do not constitute noncompliance. For example:

- A subject cannot attend an appointment which results in a change in timing of study procedures (when the change does not adversely affect risk to subjects);
- An ineligible subject is enrolled in the study due to misinformation provided to the researcher;
- Exceeding the number of subjects in a study in limited circumstances when enrollment is outside the control of the researcher, (e.g., responses to a recruitment flyer with a link to an online survey exceed the number expected; in this case, the researcher cannot control who sees the flyer, how many individuals choose to respond, etc.).

**Noncompliance in Exempt research:** Research granted exempt status is subject to fewer regulatory requirements than non-exempt research. For example, some changes to an exempted protocol can be implemented without prior IRB review. In general, noncompliance in exempt research involves the following:

- Initiating human subjects research activities prior to receiving a written determination of exemption from the Office of Research Ethics.
- Deviations from an exempted protocol that alter the exempt status of the study or are contrary to IRB guidance [Modifications to Exempt Research](#).

Noncompliance in exempt research is reviewed in accordance with the procedures outlined in this document. However, consideration is given to the flexibility afforded to exempt research when determining whether an incident constitutes noncompliance.

**Minor noncompliance:** Noncompliance that does not rise to the level of *serious* or *continuing* noncompliance. Minor noncompliance typically involves administrative oversights, non-substantive unapproved changes, etc. Noncompliance that does, or reasonably may, adversely affect the rights, safety, or welfare of research subjects is **not** minor, even if no actual harm has occurred. Examples that may be deemed minor include, but are not limited to:

- Implementing non-substantive changes to approved procedures without IRB approval, such as:
  - Re-wording survey or interview questions where the meaning and scope of the question does not change;
  - Wording changes in recruitment materials or consent forms that do not change the meaning of the information provided or result in excluding any required element(s) of consent;
  - Changing the order in which study conditions are administered, as long as a specific order is not necessary to minimize risk;
  - Enrolling subjects who do not meet the inclusion or exclusion criteria, except in the circumstances described as serious noncompliance below.

- Exceeding the approved number of subjects in a study
- Unapproved changes in study personnel, when the changes do not alter the qualifications of the overall research team and all personnel have completed required human subjects protection training.

**Serious noncompliance:** Noncompliance that compromises the safeguarding of the rights, safety or welfare of human research subjects, or that does or may reasonably adversely affect the rights, safety, or welfare of human research subjects, even if no actual harm occurred. Acts that are determined by the IRB to be flagrant or intentional violations of IRB requirements may also constitute serious noncompliance. The IRB will consider the circumstances surrounding the case when making a decision related to serious noncompliance. In general, examples of serious noncompliance include, but are not limited to:

- Failure to obtain IRB approval or determination of exemption prior to initiating research activities with human subjects;
- Allowing unqualified or untrained individuals to perform research procedures or monitor subject safety;
- Failure to obtain informed consent or failure to provide participants with all information necessary to constitute meaningful informed consent unless a waiver has been previously granted by the IRB;
- Enrolling a child in a research study without the informed consent of a parent or legal guardian unless parental consent was previously waived by the IRB;
- Enrolling subjects from a vulnerable population (i.e., children, prisoners, cognitively impaired individuals, subordinates, etc.) when their inclusion is not described in the IRB-approved protocol and appropriate protections are not in place;
- Enrolling subjects who do not meet the approved eligibility criteria when doing so compromises the safety or well-being of the subjects;
- Failure to follow approved measures for protecting privacy and confidentiality when the failure presents any risk of harm to the research subject (such as harm to their reputation, social or psychological harm, risks of legal or civil liability, embarrassment, harm to workplace or family relationships, etc.);
- Implementing unapproved changes to research activities that increase risks to participants or adversely affect their rights, safety, or welfare (e.g., adding survey questions that collect sensitive information, substantially increasing the duration or intensity of exercise activities, adding plans to collect data from private records without subject consent, changes to confidentiality protections, etc.);
- Failure to report serious adverse events or unanticipated problems involving risks to subjects or others as required by IRB policy;
- Instructing or knowingly allowing subordinates (e.g., research assistants, employees, students, etc.) to engage in activities that are contrary to IRB or institutional policies or regulatory requirements;
- Providing false or intentionally misleading information to the IRB;
- Multiple issues suggesting a lack of oversight, inaction, or negligence such that research subjects' rights, safety, or welfare could be adversely affected.

**Continuing noncompliance:** Repeated acts of noncompliance in the conduct of human subjects research suggesting a pattern indicative of a lack of understanding or attention to adequate safeguarding of the rights, safety, or welfare of human subjects or of university policies and/or non-university regulatory requirements for the conduct of human

subjects research. Continuing noncompliance is characterized by the frequency rather than the magnitude of the noncompliance. Examples of continuing noncompliance include, but are not limited to:

- Repeated failure to obtain IRB approval prior to initiating human subjects research activities;
- Continuing to engage in noncompliant activities after being notified or advised of concerns;
- Recurring late submissions of continuing review applications resulting in repeated lapses in approval;
- Multiple instances of serious or minor noncompliance; this includes multiple incidents within a single project or multiple incidents by a single investigator across more than one project.
- Failure to respond to incidents of noncompliance or failure to enact required corrective actions.

## Policy

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All instances of noncompliance must be promptly reported to the IRB chair(s) or ORE staff. Written reports are preferred, although reports by telephone are acceptable. Instances involving actual or imminent harm to research subjects or others must be reported immediately.

Reports of noncompliance may come from many sources. The PI may self-report noncompliance and is encouraged to do so. Self-reporting will be looked upon favorably during assignment of corrective actions. In other cases, a research subject may submit a complaint, a member of the research team may report an incident, or an incident may be discovered during IRB review or post-approval monitoring. Research staff who become aware of potential noncompliance should notify the PI as soon as possible. In cases where research staff prefer not to notify the PI, reports can be submitted to [IRB@iastate.edu](mailto:IRB@iastate.edu). Alternately, any individual may report concerns to [ISU's Compliance and Ethics Hotline](#).

Instances discovered during IRB review or via post-approval monitoring are reported by IRB staff as indicated in this policy.

A PI may also be required to report incidents to his/her department or the study sponsor; PIs are responsible for knowing reporting requirements that may exist beyond those specified by the IRB and for following those requirements.

## Informal Resolution for Specified Minor Noncompliance

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The IRB has predetermined that one-time or isolated cases of the following types of incidents constitute minor noncompliance and can be resolved by IRB staff:

1. Over-enrollment in a minimal risk non-exempt study.
2. Unapproved changes to personnel, other than the PI or Supervising Investigator, when:
  - a. Any new personnel have completed required human subjects protection training before being involved in human subjects research activities, or
  - b. Removal of personnel does not adversely affect the qualifications of the research team or its ability to safely carry out the research.

3. Unapproved changes in the type of compensation (e.g., changing from cash to gift cards), when the change does not alter:
  - a. the amount of compensation; and
  - b. plans for pro-rating compensation; and
  - c. privacy or confidentiality provisions (e.g., no changes to the collection of identifiers, whether identifiers are connected to data, etc.).

IRB staff assess the totality of the circumstances regarding the incident. If they determine the incident is eligible for informal resolution, it is handled as follows:

1. Verify the incident is a one-time or isolated case by checking IRB records. Repeated incidents associated with a PI or project may constitute continuing noncompliance, and are not eligible for informal resolution.
2. Rectify the issue by advising the PI (and Supervising Investigator) to
  - a. promptly obtain IRB approval by submitting an Amendment for Modification if they have not already done so; a reasonable deadline for completing this step should be established if appropriate; and
  - b. adhere to the approved protocol until the Amendment for Modification receives IRB approval (if appropriate).
3. Educate the PI (and Supervising Investigator) by informing them of the minor noncompliance and reminding them that IRB approval must be obtained for any changes prior to implementation.
4. Document the incident as a minor noncompliance event in IRBManager. Documentation supports identification of patterns of noncompliance.

The incident will be forwarded for review in accordance with the IRB Review Process outlined in the next section if:

1. IRB staff determine the incident is not appropriate for informal resolution; or
2. The PI does not address the issue within a reasonable timeframe.

## IRB Review Process

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Incidents not meeting the criteria for informal resolution are handled as outlined in the remainder of this document. Upon receipt of a report of potential noncompliance, IRB staff forward the information to the IRB Co-Chair/designee.

In cases involving serious harm to subjects or where immediate action is needed to prevent such harm, the DORE should also be informed. Other responsible parties should be consulted if the IRB Co-Chair and/or DORE are unavailable. These individuals may include the IRB Chair or Vice-Chair, Associate Vice President(s) (AVPR) for Research and/or the Vice President for Research (VPR) who serves as Institutional Official (IO).

### Initial review

The IRB Co-Chair, in consultation with the DORE and IRB Chair(s) as needed, conducts a preliminary evaluation of the allegations/concerns to determine whether the allegations are based in fact. If the allegation/concern is unsubstantiated, no additional action is needed. If the incident is based in fact, a preliminary assessment is made related to whether the issue involves noncompliance. When needed, additional information is gathered at this stage.. The VPR or AVPR may be consulted when necessary (e.g., additional resources are needed to adequately complete

the investigation, the incident may also involve academic misconduct, etc.). Temporary suspension of IRB approval may be enacted by the parties involved in the initial review if deemed necessary to prevent harm to subjects.

## Subcommittee review

Review of the incident is next referred to the IRB Compliance Subcommittee consisting of the DORE, IRB Chair, Co-Chair, and Vice-Chair; the Subcommittee reviews the allegations and related materials to determine whether an incident constitutes noncompliance. If an incident is determined to constitute minor noncompliance, corrective actions to resolve the noncompliance are imposed by the Subcommittee. Corrective actions may include, but are not limited to:

- Acknowledgement of the report with no further action needed;
- A warning or reminder to the PI with instructions on how to avoid future incidents, clarifications regarding requirements and rules, etc.;
- Requiring additional human subjects protection training;
- Requiring submission of an amendment or report of an adverse event/unanticipated problem;
- Requiring the PI to submit a corrective action plan;
- Directing post-approval monitoring visits;
- Directing compliance audits.

The DORE communicates outcomes of Subcommittee review to the PI. If the PI complies with the corrective actions, additional review by the convened IRB is not required.

A report summarizing the incident(s) and outcome(s) is provided to the convened IRB for review and concurrence. If the convened IRB disagrees with the Subcommittee's determination of minor noncompliance, it may require additional information or further review by the convened IRB.

## Convened IRB review

Review of the incident is referred to the convened IRB review when:

1. it is determined during the initial review that the incident may involve serious or continuing noncompliance, or
2. there is uncertainty or disagreement by the initial reviewers about the level of noncompliance, or
3. the investigator fails to cooperate with the actions required to correct minor noncompliance, or
4. the IRB disagrees with the Subcommittee's determinations.

A report describing the potential noncompliance case, along with relevant materials, is shared with the IRB. The PI is informed of the IRB's review and invited to attend the meeting to discuss the report with the IRB. Reasonable efforts are made to accommodate scheduling needs of the PI.

If the facts of the case raise serious concerns about the rights, safety, or welfare of participants, the IRB may suspend approval of the research while the case is under review.

The IRB issues a formal determination of the type of noncompliance (i.e., serious and/or continuing). If the IRB determines that neither serious nor continuing noncompliance has occurred, the IRB may dismiss the allegations or determine the noncompliance is minor and delegate handling of corrective actions to the DORE.

If the IRB determines that serious and/or continuing noncompliance has occurred, the IRB recommends corrective actions for consideration by the Institutional Official. When appropriate, a reasonable timeframe for implementation of these actions should be established. Recommendations may include, but are not limited to:

- Providing a warning or reminder to the PI with instructions on how to avoid future incidents, clarifications regarding requirements and rules, etc.;
- Requiring additional human subjects protection training for the PI/research team;
- Requiring the PI to submit a corrective action plan;
- Recommending that the Institutional Official (or designee) work with the PI's department chair/head or Director of Graduate Education (DOGE) to determine appropriate actions regarding the data collected as a result of the non-compliant actions;
- Directing post-approval monitoring visits;
- Directing compliance audits;
- Restricting the ability to serve as PI on human subjects protocols (e.g., requiring a supervising co-PI, barring future eligibility as PI, etc.);Notifying study participants;
- Requiring that participants are given the option to re-consent to participation.

The IRB may also require modifications to the protocol or informed consent process, more frequent continuing review, or that all future submissions be reviewed by the convened IRB. The IRB may also suspend or terminate approval of protocols found to be noncompliant if deemed necessary to protect human subjects. The welfare of currently enrolled subjects is taken into account when considering suspension or termination of approval.

The IRB may refer the issue to other organizational entities, such as legal counsel, risk management, the Research Integrity Officer, etc., in lieu of or in addition to the recommended corrective actions.

Principal Investigators are encouraged to play an active role in the noncompliance review process. The PI is provided with an opportunity to review and comment on noncompliance reports provided to the IRB for consideration. PI comments must be received by the deadline established by the DORE to be included with information provided to the IRB. The PI will be invited to address the IRB during the meeting where the noncompliance review occurs. A report summarizing the IRB's determinations and recommended corrective actions will be provided to the PI for review and comment prior to submission to the Institutional Official for consideration of corrective actions. Comments must be provided by the deadline established by the DORE. The PI's comments will be forwarded to the IRB for reconsideration if the comments reveal new factual information or other circumstances that are reasonably likely to affect the IRB's determinations or recommendations.

## Institutional Official review

In cases of serious or continuing noncompliance, the Institutional Official receives a final report documenting the noncompliance review process, the IRB's recommendations, and any response to these recommendations by the PI. The Institutional Official may accept, revise, add to, or reject any or all of the IRB's recommended corrective actions but may not change the IRB's determinations related to the level of noncompliance or overturn the IRB's decision to suspend or terminate IRB approval, to require modifications to the approved protocol, or to require more frequent or higher-level IRB review. The final report documenting the Institutional Official's actions is provided to the PI, the PI's department chair/head, the Associate Dean for Research of the PI's college, supervising faculty (if applicable), the IRB Chair(s), and for the IRB files. Other internal and external reporting requirements are outlined below.

## Other review

There may be instances where noncompliance rises to the level of academic or research misconduct. Academic or research misconduct charges are processed in accordance with ISU policies.

## Appeal to the VPR/IO of noncompliance actions

Grounds for appeal to the Vice President for Research are limited to 1) a violation of university rules, regulations, policies; or 2) a specific act by the university that was arbitrary or capricious. Such appeals must be filed within 10 business days of the date the final noncompliance report is sent to the PI. The Vice President for Research will respond in writing within 30 business days of receiving the appeal, unless, in the opinion of the Vice President, that is insufficient time to appropriately investigate and consider the substance of the appeal. If additional time is needed, the Vice President shall contact parties to provide a new date by which the decision shall be made.

## Follow-Up

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Principal investigators are responsible for ensuring the corrective actions outlined in the final noncompliance report are implemented by the timeframes established in the report. The Post-Approval Monitor (PAM) oversees the progress of implementation with the assistance of the DORE and IRB Co-Chair as needed. Failure to meet the conditions established in the report will result in additional review by the IRB and possible termination or suspension of IRB approval.

## Internal reporting

The PI's department chair and the Associate Dean for Research of the PI's college are provided a copy of the finalized report in cases determined to be serious or continuing noncompliance. Other ISU offices are informed of the IRB's noncompliance review as necessary to conduct the review or meet reporting requirements. For example, the Office of Sponsored Programs Administration may be contacted for advice on requirements for sponsored research related to reporting noncompliance.

## External reporting

When applicable, incidents of serious or continuing noncompliance must be reported to the Office of Human Research Protections per the requirements set forth in 45 CFR 46.103(b)(5) and the funding agency or sponsor in accordance with their requirements. Similarly, reports of serious or continuing noncompliance must be provided to the Food and Drug Administration for FDA-regulated research in accordance with 21 CFR 56.108(b), 21 CFR 56.113, 21 CFR 812.150. When appropriate, preliminary reports may be filed pending final resolution of the case.

### Document History

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