

Non-Compliance Involving Human Subjects' Research

Introduction:

This policy describes the process that the IRB follows to manage allegations and findings of non-compliance with human subject protection regulations.

Definitions:

Allegation of non-compliance: An unproven assertion of non-compliance; suspected non-compliance with human subject protection regulations.

Continuing Non-Compliance: A pattern of non-compliance that, in the judgment of the IRB Chair or convened IRB, indicates a lack of understanding of the regulations or institutional requirements that may affect the rights and welfare of participants, would have been foreseen as compromising the scientific integrity of a study such that important conclusions could no longer be reached, suggests a likelihood that non-compliance will continue without intervention, or frequent instances of minor non-compliance. Continuing non-compliance also includes failure to respond to a request to resolve an episode of non-compliance with human subject protection regulations.

Finding of Non-compliance: A formal designation of non-compliance with human subject protections as determined by the IRB (a fully convened committee, the IRB Chairperson or designee).

Minor Non-Compliance: Non-compliance that is neither serious nor continuing. An example of minor non-compliance includes failure to comply with UHCMC IRB policies that is administrative in nature (for example, turning in a report of an unanticipated problem a day late, failure to date a consent form or use of a consent form contextually identical to the IRB approved consent form, but without the presence of the IRB approval stamp).

Non-Compliance: Any action or activity associated with the conduct or oversight of research involving human subjects that fails to comply with federal regulations or the requirements or determinations of the IRB. Non-compliance actions may range from minor to serious, be unintentional or willful, and may occur once or more than once. The degree of non-compliance is evaluated on a case-by-case basis and will take into account such considerations as to what degree subjects were harmed or placed at an increased risk and willfulness of the noncompliance. Examples include, but are not limited to: Failure to obtain IRB approval; inadequate or non-existent procedures for the informed consent process; inadequate supervision; failure to follow recommendations made by the IRB; failure to report adverse events or protocol changes; failure to provide ongoing progress reports; or protocol deviations.

Serious Non-compliance: An action or omission in the conduct or oversight of research involving human subjects that affects the rights and welfare of participants, increases risks to participants, decreases potential benefits or compromises the integrity or validity of the research. Examples of serious non-compliance include, but are not limited to: conducting research involving human subjects without IRB approval; enrollment of subjects that fail to meet the inclusion or exclusion criteria of the protocol, that in the opinion of the IRB Chair, Vice Chair(s), or convened IRB increase the risk to the subject; or enrollment of research subjects while study approval has lapsed; or major protocol deviations that may place subjects at risk from the research.

Policy:

The IRB, as part of their oversight responsibilities must establish procedures for the evaluation of all non-compliance with human subject protection regulations and institutional policies and the prompt reporting of any serious or continuing non-compliance with the Federal regulations or institutional policies. The UHCMC IRB requires investigators to report all matters of potential non-compliance to the IRB. If an allegation of non-compliance is reported from any source (including monitoring/auditing reports, subject complaints, internal allegation or investigator self-reporting), the UHCMC Office of Research Compliance (ORC) in consultation with the IRB Chair or Vice-Chair, and Vice President for Research will make an initial assessment to determine:

- (i) whether there is sufficient information present to verify and determine if the allegation is true;
- (ii) whether additional information is needed to make a determination; and
- (iii) whether a determination of non-compliance, is serious or continuing non-compliance.

All reports of alleged non-compliance or inappropriate involvement of humans in research are investigated by the Research Compliance Office. If it is determined that the non-compliance might be serious or continuing, the suspected non-compliance is forwarded to a convened meeting for full Board review and determination.

Goals of the Research Compliance Office and the IRB in investigating and managing issues of potential noncompliance include:

- a) Assuring the safety, rights and welfare of human subject research participants;
- b) Developing action plans to prevent recurrence, and promote a culture for future compliance;
- c) Educating research staff to assure the understanding of DHHS (OHRP) and FDA regulations and guidelines, and UHCMC IRB Policy; and
- d) Reporting serious or continuing noncompliance to the appropriate regulatory agencies and institutional officials.

Instances meeting the definition of research misconduct will be reported to the Vice President for Research (*see* [UHCMC Policy AP&P II 16.6, Scientific Misconduct in Research](#)).

A) Identification and Investigation of Non-Compliance

An allegation of non-compliance will result in the Research Compliance Office conducting an investigation of the suspected non-compliance. Allegations and/or findings of non-compliance are identified in a variety of ways including notification by investigators, research team members, regulatory bodies, sponsors, research participants, institutional personnel or committees, the public or anonymous sources. The initial allegation may be presented orally; however, a follow-up written statement of the allegations is required. At the discretion of the Vice President for Research and the IRB Chair, and Vice Chair(s) (or appointed designees), the requirement for a written allegation may be waived. Findings of non-compliance may also be identified during monitoring visits conducted by the Office of Research Compliance and Education.

Unsolicited or Voluntary Notifications of Allegations or Findings of Non-Compliance

When findings and allegations of non-compliance are reported to the Center for Clinical Research and Technology, it is initially reviewed by the Research Compliance Office. Research Compliance personnel will review the documentation and request additional information, as needed. The UHCMC Office of Grants and Contracts will be notified of the investigation if that office is responsible for managing any related grant funding to the protocol in question. If a detailed explanation does not accompany the report, the Research Compliance Office will contact the principal investigator to request additional information. The investigation will begin within 5 working days of learning of the recognized concern. The purpose of the investigation is fact-finding, and may involve examination of study records and discussion with investigators, the research team, other personnel, research participants, and others as appropriate. A communication will be sent to the principal investigator describing the issue or allegations, any interim immediate action, and a request for additional information and response from the investigator.

If requested by the individual reporting the allegation, the Research Compliance Office and ultimately the IRB will attempt to keep his or her identity confidential; however, confidentiality cannot be assured. If an anonymous allegation is made, the Research Compliance Office, the Vice President for Research, the IRB Chair, and ultimately the IRB will decide if sufficient detail is available to determine if non-compliance has in fact occurred and whether the allegation can be investigated in the absence of an identified complainant.

If an allegation of non-compliance is initially communicated to the Office of Research Compliance at Case Western Reserve University (Case) or if the allegation is related to funding awarded to Case for a human subject protocol, the Case Office of Research Compliance and the Case Office of Sponsored Projects will be kept informed of the

progress of the review and notified of the IRB meeting at which the case will be discussed.

Allegations or Findings Identified by the ORC

Allegation or Findings of non-compliance identified during monitoring visits conducted by the Office of Research Compliance and Education are reviewed with the IRB Chair. Prior to reviewing the findings with the IRB chair, the ORC will prepare a written summary of the observations and propose an action plan for the investigator. Upon review of the summary and action plan with the IRB Chair, the action plan may include any, or all of the following:

- Asking the investigator to submit a Protocol Deviation/Unanticipated Problem to the IRB for further review;
- Identifying the finding as minor non-compliance and request a thorough action plan to correct and/or prevent the event from occurring again;
- Require Education;
- Require additional monitoring

Once the IRB Chair is in agreement with the proposed action plan, the Investigator will receive the post monitoring letter that includes all monitoring observations, proposed action items, recommendations, educational requirements, and additional monitoring requests from the ORC.

B) Minor Non-Compliance

The Research Compliance staff will try to resolve reports of minor non-compliance with the principal investigator and research team. If the Research Compliance staff cannot work out a corrective action plan with the principal investigator, then the report will be referred to the reviewing IRB for recommendations.

Allegations of minor non-compliance will be investigated by the Research Compliance staff by contacting the principal investigator and research team for verification. Research Compliance staff that receives allegations or reports of noncompliance will conduct the initial fact-finding and compile information regarding the noncompliance. If noncompliance is clearly minor and the proposed action plan seems adequate, Research Compliance staff may handle the allegation or report by documenting the event and the proposed corrective action and reporting the incident to the IRB Chair, Vice Chair(s) (or designee). No further action is required. If, in the course of handling the allegation or report of noncompliance, Research Compliance staff is concerned that the noncompliance may be serious or continuing, the matter will be referred to the Vice President for Research, IRB Chair, Vice Chairs (or designees) for further action as established in policy section "IRB Review of Allegations of Serious or Continuing Non-Compliance". As soon as possible and generally within fifteen (15) days of the completion of the initial fact gathering process (unless additional time is authorized by VP Research/Chair/designee), the Chair/designee will issue one of the following determinations:

Not noncompliance

When the Chair/designee determines that the facts do not support a finding of noncompliance as defined in this Policy, the report of noncompliance will be dismissed and no further action will be taken under this Policy. The affected investigator(s) will be notified in writing of the determination.

Minor noncompliance

When the Chair/designee determines that the facts support a finding of minor noncompliance as defined in this Policy, the Chair/designee will either approve the research to continue with no further action required or require modifications that do not constitute more than a minor change in the research.

The affected investigator(s) will be notified in writing of the determination and the facts supporting the determination. No further action will be taken under this Policy unless the investigator refuses to cooperate with the corrective action. Any required changes or modifications submitted by the investigator in response to the determination shall be reviewed by the UHCMC IRB according to applicable policies on review of proposed changes in approved research.

It is generally expected that these will be eligible for review according to the policy on review of minor changes in approved research using the expedited review procedure.

C) IRB Review of Allegations of Serious or Continuing Non-Compliance

When the IRB Chair (or designee) determines the information regarding an alleged report of non-compliance is serious, the information is forwarded to the full IRB for review, consideration of suspension criteria, or consideration of termination. An investigation by the Research Compliance Team can occur simultaneously with IRB review for consideration of suspension. If the IRB Chair, Vice Chair(s) (or designees) has suspended the research because of findings or alleged findings of serious or continuous non-compliance, the IRB will vote to confirm or reverse that decision.

Any voting member of the IRB or the Vice President for Research (or designees) will serve as primary and secondary reviewers and present the materials at the convened IRB meeting. The IRB will then:

1. Review the information (provided in B. above);
2. Vote on the information provided as indicated in 3 and 4 as follows, or defer the vote and gather additional information if needed from the investigator or others involved;
3. Vote on whether the non-compliance is serious; and
4. Vote on whether the non-compliance is continuing

The discussion, determination, and vote will be recorded in the IRB meeting minutes. The minutes must also include a description of the non-compliance issue and allegations and also document the vote as to whether the study is to continue with or without change, is suspended, or is terminated and whether corrective action is required.

Unless otherwise approved by the IRB Chair or Vice Chair(s), no visitors may be present during the portion of the IRB meeting when a non-compliance matter is discussed. If a member of the IRB has or declares a conflict of interest regarding a specific investigator or protocol scheduled for a compliance discussion, he or she will leave the meeting while the non-compliance issue is discussed and will not vote on the issue.

Format of Non-Compliance Report Reviewed by the IRB

To assist in making a determination, a report outlining the facts surrounding the allegation, appropriate supporting documentation, and corrective action will be forwarded to all members of the IRB for review prior to the meeting. The following documents will be forwarded to all IRB members:

- A statement of the non-compliance allegation;
- Supporting documents including a copy of the current IRB approval letter, protocol and consent form (as applicable to the investigation);
- A statement of previous IRB administrative actions related to the non-compliance;
- Any relevant additional information or special circumstances;
- Assessment of increased risk (if any) to subjects resulting from the non-compliance;
- Recommendations for possible actions or resolution;
- Review of the status of the investigator's other IRB approved protocols;

Additionally, the primary and secondary reviewers receive:

- The current IRB approved Investigator's Brochure, if applicable;
- The Grant, if applicable; and
- Any pertinent information (e.g., questionnaires, DSMB reports, etc)

After voting, the IRB may require:

- No action, protocol continues as previously approved;
- Modification of the study protocol;
- Modification of the informed consent process;
- current participants to re-consent to participation;
- Providing information about the non-compliance to current study participants;
- Additional information be provided to past participants;
- Obtaining more information pending a final decision;
- Modification of the continuing review schedule;

- Additional training of the investigator or research team;
- Monitoring the research;
- Monitoring the consent process;
- Suspension of the research;
- Termination of the research;
- Destruction of data collected at the time the non-compliance event occurred;
- Withdrawing or limiting the privileges of the investigator to conduct human research;
- Referral to other Organizational entities (Compliance and Ethics, General Counsels, risk management); and/or
- Other actions deemed appropriate.

The principal investigator will receive written notification from the IRB via the Vice President for Research, regarding the non-compliance issue, including recommendations for corrective actions. The Research Compliance Office will maintain a separate file, including documentation and correspondence, on each non-compliance issue brought to the IRB for review.

An IRB determination of serious or continuing non-compliance will be reported to the appropriate regulatory agencies and institutional officials, (following [IRB Policy, Reporting to Regulatory Agencies, Department Heads and Institutional Officials](#)).

The IRB Chair or Vice Chair(s) using the expedited review process will review and approve all minor modifications to previously approved research received in response to non-compliance. All modifications that are determined by the Board to be more than minor will be reviewed at a convened IRB meeting.

D) Suspension or Termination

If, in the opinion of the IRB Chair, the allegation concerns non-compliance that might be serious or continuing, the IRB Chair, Vice Chairs (or designees) may suspend research activities immediately until such time that the full IRB can convene if they believe that research participants may be exposed to immediate harm. If the Chair, Vice Chairs (or designees) is unavailable, and in the opinion of the Vice President for Research, the allegation concerns non-compliance that might be serious or continuing, the Vice President for Research may suspend research activities immediately (following [IRB Policy, Administrative Hold, Suspension, or Termination of IRB Approval](#)) until such time that the full IRB can convene if it is believed that research participants may be exposed to immediate harm.

Suspension or termination of IRB approval of research will be reported to the appropriate regulatory agencies and institutional officials (following [IRB Policy, Reporting to Regulatory Agencies, Department Heads and Institutional Officials](#)).

E) Additional Considerations for Non-Compliance Issues

1) Continuing Non-Compliance or Serious Non-Compliance

If the investigator is a member of the faculty of Case and the research involves a Federal grant, or other grants awarded to Case, or the non-compliance is determined to be serious or continuing, the IRB may refer the issue of non-compliance to the Associate Vice-President of Research at Case for assistance in seeking an appropriate resolution (*see [Institutional Advisory Committee Policy on Human Subject Noncompliance](#)*).

If the investigator is a member of the medical staff of UHCMC, a continuing non-compliance issue may be referred to the Chief Medical Officer for assistance in seeking an appropriate resolution.

2) Non-Compliance with HIPAA (Privacy Language) Requirements

Failure to comply with HIPAA (Privacy Rule) requirements for research studies will not be treated as a non-compliance issue by the IRB. Instances of non-compliance with HIPAA requirements will be referred to the UHCMC Privacy Officer for investigation and resolution that may include review by the UHCMC Research Privacy Board.

References and/or Regulatory Citations:

[45 CFR 46.103\(b\) \(5\)](#)

[45 CFR 46.113](#)

[21 CFR 50](#)

[21 CFR 56](#)

Related Policies:

[IRB Policy, Administrative Hold, Suspension, or Termination of IRB Approval](#)

[IRB Policy, Reporting to Regulatory Agencies, Department Heads and Institutional Officials](#)