

Case Cancer Institutional Review Board Policy

Non-compliance with Regulations of Human Subject Research

Purpose

To describe the IRB process for ensuring that non-compliance with federal regulations, state laws and local laws and policies or with the requirements or determinations of the Case Cancer IRB will be reported to the Case Cancer IRB, evaluated and appropriately addressed.

Definitions

Non-compliance: Failure to comply with any applicable federal, state and/or local laws and 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 non-compliance.

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

Serious Non-compliance: Any non-compliance that significantly negatively impacts or affects the rights and welfare of subjects or others, increases the risks to participants, decreases potential benefits to participants, or compromises the integrity or validity of the study data.

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 or others, and may be foreseen as compromising the scientific integrity of a study such that there is the potential of affecting the rights and welfare of subjects or others, increasing risks to participants, decreasing potential benefits to participants, or compromising the integrity or validity of the study data and/or suggests a likelihood that non-compliance will continue without intervention. Continuing non-compliance also includes failure to respond to a request by the IRB to resolve an allegation of non-compliance.

Process

Reporting allegations of non-compliance

Investigators must report all non-compliance to the Case Western Reserve University (Case) School of Medicine (SOM) Office of Research Administration (ORA). Allegations of non-compliance also may be reported by any other source including research team members, regulatory bodies, sponsors, research participants, institutional personnel or committees, the public or anonymous sources. Allegations should be directed to the Case SOM ORA. The initial allegation may be presented orally; however, a follow-up written statement of the allegations should be completed. The information submitted in the allegation should ideally be as specific as possible, and should include a description of the non-compliance, persons involved, and the date(s) the non-compliance occurred.

Initial Review

The Case SOM ORA in consultation with the IRB Chair or IRB Vice-Chair will obtain information from the principal investigator, study staff and regulatory personnel at the

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site and then make an initial assessment as to whether non-compliance occurred and if so, whether the non-compliance appears to be serious or continuing.

Unsupported Allegations

If the IRB Chair or IRB Vice-Chair and the IRB Administrative Director determine that the allegation is not a matter of non-compliance, the Case SOM ORA shall maintain a copy of the records and determination.

Non-Compliance that is neither serious nor continuing

If the allegation is found to be non-compliance that is neither serious nor continuing and the Principal Investigator along with the Case SOM ORA has created a corrective and/or preventative action plan that is adequate in the opinion of the IRB Chair and IRB Administrative Director, the Case SOM ORA shall document the event and the proposed corrective action administratively, and then report the finding and corrective action to the full Board as an administrative action. The full Board shall vote to accept. If the Board does not accept, the allegation shall be further investigated as if it appeared to be serious or continuing non-compliance.

If the Case SOM ORA cannot adequately investigate the allegation or work out a corrective action plan, the Case SOM ORA will contact the Research Compliance Office of the Principal Investigator's institution and they will work together to complete the review and develop a corrective action plan. If working together, these offices cannot complete the review or come to an agreed corrective action plan within a reasonable period of time the allegation will be reported to the convened IRB with recommendations for further action.

Administrative reviews will be kept in the IRB Records and communications to the principal investigator(s) will be sent with any recommended corrective action plan or recommend educational activities in order to prevent re-occurrence, and promote a culture for future compliance.

The IRB Chair or Vice Chair(s) using the expedited review process will review and approve all minor modifications to previously approved research taken in response to non-compliance. All modifications that are determined to be greater than minimal risk to subjects or include a significant change in study design will be reviewed at a convened IRB meeting.

Allegations of Serious or Continuing Non-Compliance

If the Case SOM ORA, or the IRB Chair or the IRB Administrative Director determines that the allegation may be considered serious or continuing non-compliance, the Case SOM ORA will report the allegation to the Research Compliance Office of the Principal Investigator's institution. The Case SOM ORA will work in conjunction with Research Compliance Office of the Principal Investigator's institution to investigate allegations of serious or continuing non-compliance. 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(s) describing the issue or allegations, any interim immediate action, and a request for additional information and response from the investigator.

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The Case SOM ORA, in conjunction with Research Compliance Office of the Principal Investigator's institution shall create a report outlining the facts surrounding the allegation, appropriate supporting documentation, and recommended corrective action. The report should include the following information:

- A description 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 determination of either not non-compliance, serious non-compliance, continuing non-compliance or serious and continuing non-compliance;
- Recommendations for possible corrective and/or preventative actions or resolution;
- Review of the status of the investigator's other IRB approved protocols;

The report shall be forwarded to the convened IRB for full Board review and consideration of sanctions, which may include suspension or termination of the research. Any non-conflicted voting member of the IRB can serve as primary reviewer and present the materials at the convened IRB meeting. All members at the convened IRB will review the information included in the non-compliance report. The member acting as primary reviewer will also receive a copy of the current IRB approved Investigator's Brochure (if applicable), the Grant (if applicable), and any pertinent information (e.g., questionnaires, DSM reports, etc.).

The convened IRB will vote on whether the non-compliance is serious, whether the non-compliance is continuing, any increased risk to subjects occurred as a result of the non-compliance, and any necessary plans for corrective action. The following are examples of the types of action(s) the convened IRB may require:

- No action, protocol continues as previously approved;
- Modification of the study protocol;
- Modification of the informed consent process;
- Modification of the information disclosed during the informed consent process;
- Require current participants to re-consent to participation (required when such information might relate to participants' willingness to continue to take part in research);
- Provide information about the non-compliance to current study participants;
- Additional information provided to past participants;
- Obtain more information pending a final decision;
- Modify the continuing review schedule;
- Require additional education and training of the investigator or research team;
- Monitoring of the research;
- Monitor of the consent process;
- Suspend the research;

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- Terminate the research;
- Destruction or continued use of data collected at the time the non-compliance event occurred;
- Withdraw or limit the privileges of the investigator to conduct human research;
- Referral to other Organizational entities (Compliance and Ethics, General Counsels, risk management, Institutional Officials); and/or
- Other actions deemed appropriate.

If the convened IRB concludes that not enough information is available to determine if the non-compliance is serious or continuing, the IRB can defer the vote and request the Case SOM ORA in conjunction with Research Compliance Office of the Principal Investigator's institution to gather additional information.

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 discuss or vote on the issue.

The principal investigator(s) will receive written notification from the IRB Office, regarding the outcome of the non-compliance issue, including required corrective actions. The Case SOM ORA will maintain in the relevant IRB records documentation and correspondence, on each non-compliance issue brought to the convened IRB for review.

An IRB determination of serious or continuing non-compliance will be reported to the appropriate regulatory agencies and institutional officials, as outlined in the IRB Standard Operating Procedures for Reporting to the Institutions and Government Agencies.

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 or Vice Chairs (or designees) may suspend research activities immediately until such time that the full IRB can convene. If the Chair or Vice Chairs (or designees) is unavailable, and in the opinion of the IRB Administrative Director, the allegation concerns non-compliance that might be serious or continuing, the IRB Administrative Director may place an administrative hold on research activities immediately (following IRB Standard Operating Procedures for Suspension or Termination of Approval of Cancer Research) until such time that the full IRB can convene.

Suspension or termination of IRB approval of research will be reported to the appropriate regulatory agencies, the Research Compliance Office of the Principal Investigator's institution and other institutional officials as appropriate following IRB Standard Operating Procedures for Suspension or Termination of Approval of Cancer Research

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An investigation of non-compliance can occur simultaneously with convened IRB review for consideration of suspension. If the IRB Chair or Vice Chair(s) (or designees) has suspended the research, the IRB will vote to confirm or reverse that decision.

Additional Considerations for Non-Compliance Issues

The applicable institution's Institutional Official, Research Administrator or Office of General Counsel may be involved or consulted in seeking an appropriate resolution. It is the responsibility of the involved institution's Research Compliance Office to notify its office of sponsored projects of the investigation if that institution is responsible for managing any related grant funding to the protocol in question.

Non-Compliance with HIPAA (Privacy Language) Requirements

Instances of non-compliance with HIPAA requirements will be referred to the Human Protections Administrator and HIPAA Privacy Officer of UHCMC and/or Cleveland Clinic, as appropriate, for investigation and resolution. The Cancer IRB shall coordinate with these entities to determine whether the non-compliance needs to be further addressed by the IRB.

Regulatory Citations

45 CFR 46.103(b) (5)

45 CFR 46.123

21 CFR 56.108 (b)

21 CFR 56.120-124