Western Carolina University
Office of Research Administration
Institutional Review Board Standard Operating Procedures

SOP# 302.1	TITLE: Non-Compliance	Date Effective: 01/01/2022 Last Revision Date: 10/24/2023

I. Purpose

This procedure sets forth the definition of non-compliance and the IRB process for assessing non-compliance and issuing corrective actions

II. Scope

All university personnel conducting research involving human subjects are expected to comply with the highest standards of ethical and professional conduct in accordance with federal regulations and institutional policies and procedures. Any member of the research team (i.e., faculty, students, staff, or anyone conducting research reviewed by Western Carolina University's IRB) may be subject to allegations or inquiries into non-compliance. Categorization of type of non-compliance will be determined by the IRB based on the totality of circumstances surrounding the event.

III. Definitions

Continuing Non-Compliance is defined as a repeated failure to adhere to the laws, regulations, policies, and procedures governing human subjects research.

OHRP has advised that it considers noncompliance to be continuing if it persists after the investigator knew or should have known about it. In such cases, the WCU IRB holds a presumption of continuing noncompliance, placing the burden on the investigator to present compelling, mitigating circumstances.

The period in which the continuing noncompliance occurred could be days or weeks (depending on the seriousness of the matter), and the IRB does not need to call an issue noncompliance before being able to call it continuing noncompliance.

Non-Compliance is defined as a failure to adhere to laws, regulations, policies, and procedures during the course of human subjects research. Noncompliance may range from relatively minor, administrative violations to serious violations that pose risks to subjects or violate the subject's rights and/or welfare.

Institutional Official: The individual at an institution with the authority to speak for and legally commit the institution to adherence to the requirements of the federal regulations regarding the involvement of research with human subjects.

Non-compliance includes, but is not limited to:

- Conducting research under an expired IRB protocol
- Initiating modifications to the protocol without IRB approval
- Enrollment of participants prior to IRB approval
- Disregarding or otherwise violating IRB-approved informed consent procedures (e.g., failing to obtain consent/assent, using unapproved or outdated consent, assent, and information sheets, missing signatures, failing to document consent process)

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.)

Serious Non-Compliance is defined as a failure to adhere to laws, regulations, policies, and procedures involving human subjects research in such a manner that involves substantive harm or risk of harm to the rights, safety, and welfare of human subjects.

Serious non-compliance may include, but is not limited to:

- Failure to obtain informed consent
- Failure to report adverse events or safety concerns to the IRB
- Purposeful disclosure of confidential information outside the research team
- Engaging in willful or knowing noncompliance
- Human subjects research conducted without IRB approval
- Substantive change to the research implemented without IRB approval

IV. Procedure

Allegations of Non-Compliance

1. Reports or complaints of non-compliance may be submitted to the IRB or to the Office of Research Administration (ORA) verbally or in writing. Reports may arise internally (e.g., from faculty, staff, investigator self-reports, ORA staff, IRB members, etc) or from external constituents (e.g., participants, regulators). The ORA/IRB will fully maintain the confidentiality of submitter, as permitted by law.

Assessment of Allegations

1. The Director of Research Compliance and the Research Compliance Officer (RCO) will review the allegation to determine whether there are any supporting documents or statements.
2. If the allegation is determined to be unsubstantiated, the Director of Research Compliance and RCO may consult with the IRB Chair or their designee. They may decide that no additional action is needed, further inquiry is necessary, or the issue should be presented to the convened IRB.
3. If the allegation is determined not to involve non-compliance, no further action will be taken.
4. If the allegation is substantiated but only involves minor or administrative issues, the RCO will contact the investigator to resolve the concern. The Director of Research Compliance and RCO will notify the IRB Chair of the report. They may decide that no additional action is needed, further inquiry is necessary, or the issue should be presented to the convened IRB.
5. If the allegation is substantiated and involves serious or continuing non-compliance, the IRB Chair will be notified, and an inquiry may proceed. If the allegation involves an increased risk of or actual serious or unexpected harm to a participant, the Chair may immediately suspend the project until the inquiry is complete (see SOP 303 Suspension and Termination).

6. At the completion of the assessment, and when it is appropriate, the RCO will communicate the IRB Chair's decision to the complainant, through the complainant's chosen mode of communication.

Inquiry into Non-Compliance

1. The Director of Research Compliance, RCO, and IRB Chair make a determination that an inquiry is necessary based on the nature and seriousness of the complaint.
2. An inquiry may also be initiated by the IRB Chair in response to *Adverse Event or Protocol Deviations/Violation* submissions by investigators in situations where multiple reports involving immediate risks to participants have been submitted to the IRB, or at the Chair's discretion.
3. The IRB Chair notifies the Principal Investigator of the inquiry in writing and conveys the nature of the complaint.
4. The IRB Chair designates a sub-committee of at least three individuals, consisting of the RCO, IRB members, and non-members as appropriate to constitute the appropriate expertise to assess the complaint.
5. The sub-committee may review any of the following:
    a. Protocol(s) specific to the complaint.
    b. Review of any sponsor audits, if available.
    c. Review of relevant study records and documents (i.e. consent forms, case reports, data records, etc.).
    d. Conduct interviews with research personnel.
6. If the PI requests or is requested to be present at a sub-committee meeting to be interviewed about the alleged non-compliance, they may be accompanied by a faculty representative, legal counsel, or another member of their department. The role of the individual is to provide support to the PI, they may not engage in the discussion between the IRB and the PI.
7. The sub-committee creates a written report of its findings and recommendations of corrective and/or disciplinary actions.
8. The results of the inquiry are reviewed at a convened IRB meeting where all IRB members will have access to relevant protocol documents and the inquiry report. The sub-committee may provide a report at the convened meeting.
9. If the inquiry suspects research misconduct, the findings are shared with the research compliance office and further investigation will follow University Policy 56: Ethics in Research.
10. If the inquiry substantiates a finding of serious and/or continuing non-compliance, the IRB votes to determine corrective action(s). Possible corrective actions include, but are not limited to:
    a. Increased monitoring of research procedures including informed consent, by IRB members or research compliance staff.
    b. Increased frequency of the continuing review cycle.
    c. Requiring additional education and training for research personnel.
    d. Requiring modifications to protocol or to the consent form.
    e. Notifying current participants of non-compliance if the information may affect their willingness to continue participation.
    f. Requiring re-consent of participants.
    g. Destruction of data.
    h. Preventing release of data to contribute to generalizable knowledge.
    i. Suspension of the study.
    j. Termination of the study.

11. The IRB notifies the Principal Investigator in writing of the determination and basis for determination. The Principal Investigator must implement the corrective actions within the specified time frame determined by the IRB. Failure to fully implement the corrective actions within the specific time frame results in the IRB suspending or terminating IRB approval for the specific study.
12. The PI has 10 days to appeal the decision in writing, if they so choose. The Institutional Official reviews the appeal and decide whether to reject the appeal or to re-open the inquiry.
13. The RCO and Director of Research Compliance assist the IRB in reporting any non-compliance determinations to external sponsors and/or regulatory agencies, if applicable to the study.
14. The IRB Chair is responsible for informing the investigator's department head, dean, and the institutional official of the corrective actions recommended by the committee.
15. When applicable, incidents of serious or continuing noncompliance must be reported to the Office of Human Research Protections 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 When appropriate, preliminary reports may be filed pending final resolution of the case.

V. Responsibilities

IRB administrators, IRB members, Investigators

VI. References

45 CFR §§ 46.103(b)(3), 46.103(b)(5), 46.113

21 CFR §§ 56.108(b)(5)

21 CFR §§ 53.113

21 CFR §§ 812.150

Borror, Kristina. Guidance on Reporting Incidents to OHRP. Webinar accessible at http://videocast.nih.gov/launch.asp?18537