



Division of Research Policy

SUBJECT: Protocol Deviations	Effective Date: 6/01/2017	Policy Number: 10.3.15 Version 2
	Supersedes: 10.3.15	Page of 1 4
	Responsible Authorities: Vice President, Research Assistant Vice President, Research Institutional Review Board Assistant Director, Research Integrity	

- I. Background
Federal Regulations (45 CFR 46.104 (b)(4)(iii), 21 CFR 56.108 (a) (4)] and ICH 3.3.7 (which governs Good Clinical Practices in research) require that changes to previously approved research be reviewed and approved by the IRB before being implemented, except where necessary to eliminate apparent immediate hazards to human subjects. Any change to a research protocol that is carried out without IRB approval is considered a protocol deviation.

- II. Purpose
This policy outlines investigator responsibilities for reporting protocol deviations associated with an IRB approved protocol at FAU.

- III. General Statement
FAU investigators are responsible for ensuring that their human subjects research protocol is carried out as approved by the IRBⁱ and in accordance with applicable Universityⁱⁱ and regulatory requirements. When research does not follow this plan, such occurrences can have a negative impact on research participants. Protocol deviations can alter the risk-benefit ratio for participants or may jeopardize in some way the safety, rights, and welfare of research participants, or the integrity and validity of the study design.

However, there are certain times when it is necessary to implement a planned deviation from the approved research plan, or continue aspects of the research during a lapse in IRB approval, to protect research participants. Regardless of the reasons behind them, protocol deviations must be reported to the Research Integrity office for a compliance assessment. The goal is to have an open dialogue and work toward a mutually agreeable solution that is consistent with institutional and regulatory responsibilities.

IV. Policy

Protocol deviations associated with an IRB approved protocol must be reported to the Research Integrity office for a compliance assessment and, if necessary, review by the IRB.

V. Definitions

Protocol Deviation: Any exception or change to a research protocol that is not approved by the IRB prior to its initiation or implementation.

*A protocol deviation may be categorized as **major** or **minor**.*

A **major deviation** is one that: a) has increased the risk and/or decreased the benefit to individual participants, or resulted in detrimental change to a participant's clinical or emotional status, or compromised the integrity or validity of the study; b) has occurred without appropriate IRB review and approval; c) is egregious or intentional; and/or d) has been determined by the IRB to be a major deviation.

A **minor deviation** is an unintentional deviation or omission from a protocol that does not impact research participant safety or does not substantially alter risks to research participants.

Continuing Non Compliance: A deviation is determined to be "continuing" if it involves repeated incidents which suggest that noncompliance will continue unless the IRB intervenes. For example, the IRB may determine that repeated minor deviations (continuing non-compliance) are equivalent in severity to a major deviation.

VI. Accountability

The Principal Investigator (PI) will be responsible for:

- Ensuring that his/her human subjects research protocol is carried out as approved by the IRB and in accordance with applicable University and regulatory requirements.
- Reporting protocol deviation(s) to the Assistant Director, RI or Assistant Vice President, Research for any protocol for which he/she has responsibility.
- Providing additional information as requested by the IRB to further investigate a report of a protocol deviation.
- Developing a corrective action and preventive action plan (also referred to as a CAPA plan for FDA regulated studies) for protocol deviations that may occur in an IRB approved protocol for which he/she has responsibility.

The IRB will be responsible for:

- Reviewing protocol deviation reports and determining if the event was a minor or major deviation and if the pattern of these events is continuing.
- Reviewing, recommending and approving corrective action plans for any reported protocol deviations.
- Suspending and terminating approval for an IRB approved protocol, if necessary, to protect the welfare of the human subjects involved.

The Research Integrity office will be responsible for:

- Receiving and assessing protocol deviation reports
- Communicating the IRB's determination and required corrective actions (if any) to the investigator in writing.
- Following up with the investigator to ensure and document that the corrective action has been taken.
- Reporting major protocol deviations to the appropriate institutional officials, federal agencies (e.g., the Office for Human Research Protection, Food and Drug Administration, etc.) or funding agency, as appropriate.

VII. Procedures

Reports of protocol deviations may come to the IRB from various sources, including a research participant, a member of the research team, or through formal or informal monitoring or auditing. Regardless of the source, the reporting and review mechanisms are as follows:

1. If a protocol deviation has occurred, whether major or minor, it should be promptly communicated to the Assistant Director, RI or Assistant Vice President, Research after the Principal Investigator learns of the incident. The report can be made by e-mail or phone. Depending on the seriousness of the deviation, the PI may be required to follow up by immediately submitting a formal report to the IRB via IRBNET.
2. Research staff (co-investigators, RAs, etc.) who become aware of a protocol deviation should notify the PI as soon as possible. If the member of the research staff prefers not to notify the PI, he/she may contact the Assistant Director, RI or Assistant Vice President, Research or report according to the University's whistleblower procedures: <http://www.fau.edu/policies/files/1.9%20Fraud.pdf> In cases where the report comes from a source other than the PI, the IRB may later ask the PI to submit a formal protocol deviation report.
3. If any changes are needed to the protocol or consent materials (e.g., to reflect permanent changes to the protocol as a result of a deviation), these should be briefly described in the report. These changes must also be submitted as a separate amendment request. The IRB may also require additional or different changes as a result of their review.
4. When a report of protocol deviation is received, the IRB or Research Integrity staff may ask the PI or other parties to provide additional information so the IRB can further investigate the deviation and ensure the report is complete.
5. The IRB will respond to a protocol deviation report relative to its level of severity. When reviewing protocol deviation reports, the IRB will determine if the event was a *minor* or *major* deviation and if the pattern of these events is continuing.

Potential actions may include but are not limited to:

- ✓ Establishing a corrective action/preventive action plan.
- ✓ Requiring investigator(s) to complete remedial training.

- ✓ Requiring research participants to be re-consented.
 - ✓ Permitting or disallowing the use of data collected during the protocol deviation.
 - ✓ Requiring more frequent IRB review of the project.
 - ✓ Limiting the investigator's human subjects research privileges.
6. IRB staff will communicate the IRB's determination and required corrective actions (if any) to the PI and any relevant parties in writing, and will follow up with the investigator to ensure and document that the corrective action has been implemented.
 7. Major protocol deviations will be reported to the appropriate institutional officials and the federal agency (e.g., the Office for Human Research Protection, FDA, etc.) or funding agency, as appropriate. Some protocol deviations may also be regarded as research misconduct according to University policy, and further action may be required.
 8. The IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with IRB policy and federal regulations or that deviates from the approved protocol. The Committee also has the authority to halt any activity that meets the definition of "human subjects research" even if the activity was not previously submitted for IRB review.

VIII. Policy Renewal Date
May 30, 2020

IX. References
45 CFR § 46.104 (b)(4)(iii) and § 46.103(b)(4)
21 CFR § 56.108 (a) (4)
ICH 3.3.7

POLICY APPROVAL

Initiating Authority

Signature: _____

Date: _____

Name: Daniel C. Flynn, Ph.D., Vice President for Research

Executed signature pages are available in the Initiating Authority Office(s)

ⁱ Note: This refers to both FAU's 2 internal IRBs and Western IRB (WIRB), which has jurisdiction over FAU's FDA regulated studies.

ⁱⁱ This includes obligations under FAU policies 10.3.12 and 10.3.13 if the study involves an investigational drug, device or biologic regulated by FDA.