IRB PROTOCOL DEVIATIONS AND VIOLATIONS POLICY

Federal regulations require the IRB to review and approve proposed changes to research studies before initiation of these changes, except when changes are "necessary to eliminate apparent immediate hazards to the subject" [45 CFR 46.103(b)(4)(iii)]. Most proposed changes are reviewed through submission of amendments. Any changes that are made to eliminate apparent immediate hazards to a subject should be reported as soon as possible after they occur as a protocol deviation or violation.

In addition, the IRB requires prompt reporting of serious or continuing noncompliance with regulations or noncompliance with the IRB's own requirements and determinations [45 CFR 46.103(b)(5)]. Deviations from the approved protocol, i.e., changes made without prior IRB approval, fall into this category of noncompliance.

Protocol Deviation

A protocol deviation is any change, divergence, or departure from the study design or procedures of a research protocol that is under the investigator's control and that has not been approved by the IRB. Upon discovery, the Principal Investigator is responsible for reporting protocol deviations to the IRB using the standard reporting form.

Any change, divergence, or departure from the study design or procedures of a research protocol that affects the subject's rights, safety, or well-being and/or the completeness, accuracy and reliability of the study data constitutes a protocol violation. Changes or alterations in the conduct of the trial which do not have a major impact on the subject's rights, safety or well-being, or the completeness, accuracy and reliability of the study data are considered minor protocol deviations.

Examples of Minor vs. Major deviations were identified and below are examples (not all inclusive) of common Protocol Deviations. However, based on protocol specific details, sometimes what may be considered minor for one study may be major in another. Please contact the IRB office if there are any questions.

Minor Protocol Deviations:

1. Use of outdated consent for a study that has been modified
2. Study visits/procedures that are either omitted, conducted outside the visit window or in a different sequence than specified in the protocol as long as this has not potentially impacted the safety and welfare of the subject
3. Recruiting more subjects than the maximum number of subjects indicated in the IRB application
4. Assent obtained but not documented in study records
5. Use of recruitment materials and processes that include small modifications from those that are approved. Please note for all the above noted events, a single or infrequent occurrence may be considered minor; however, if it is discovered these events have involved a majority of research subjects or the frequency is increasing, this may signify a more systemic problem with the conduct of the research and this could lead to reclassification of the events as Major.

Major Protocol Deviations:

1. Failure to obtain informed consent (and assent when required) prior to initiating research procedures
2. Performing study procedures not approved by the IRB unless to eliminate immediate potential harm to the subject or others
3. Failure to perform a test approved in the protocol that is important to subject safety or study wide data integrity

4. Drug medication (dosing and dispensing) errors regardless of whether a subject was negatively impacted
5. Failure to report a serious, unanticipated adverse event that is thought to be related to the research
6. Failure to use a recruitment process not included approved by IRB
7. Enrollment of new subjects after IRB approval has expired
8. Enrolling a subject that does not meet inclusion/exclusion criteria
9. Enrollment of a subject included in a protected population that was not approved by the IRB

What/When to Report Events to the IRB

Although a deviation may not fit within one of the above categories, it may have the potential to result in a negative outcome which classifies the event as major. Investigators will need to use their judgment when making this determination.

- Major deviations must be reported to the IRB immediately and paperwork should be completed and submitted to the IRB chair within 5 calendar days of the discovery using the Major Deviation Report form.
- Minor deviations must be reported to the IRB immediately and paperwork should be completed and submitted within in 5 calendar days.

IRB Determinations about Noncompliance

If the IRB makes an initial assessment of the noncompliance report as representing potentially serious or continuing noncompliance as defined above, the committee renders a preliminary determination. The investigator is then provided with an opportunity to respond to this preliminary finding and provide additional relevant information or detail any potential mitigating circumstances that might not have previously been considered. The IRB will review this response and make a final determination regarding the noncompliance.

If the IRB makes a final determination that a report constitutes serious and/or continuing noncompliance, it must also make recommendations regarding whether the Institutional Official will report the noncompliance to the OHRP, the VA, the FDA and any other federal department or agency that funds or supports the research in which the noncompliance occurred.

In addition to making a determination of serious and/or continuing noncompliance, the committee also must decide what further action is required. The Dean of faculty (VPAA) will be notified and will assist with the action process if warranted.

Possible Actions related to the protocol can include:

1. Requesting the investigator make modifications to the protocol
2. Requiring more frequent review of the protocol (e.g., more often that the minimal of annual review)
3. Requesting the investigator modify the consent process or consent documents
4. Requiring the investigator to provide additional information to current and/or past participants or re-consenting to participation
5. Requesting further corrective actions by the study team
6. Reconsideration of IRB approval
7. Implementation of monitoring of the research
8. Implementation of monitoring of the consent process
9. Suspension of the research study/project(s)
10. Termination of the research study/project(s)
11. Additional education for the investigator and/or the research team
12. Referral of the matter to the Institutional Official for further consideration

The IRB may require additional action, such as protocol or consent form revisions, even without a finding of serious or continuing noncompliance.
**NOTE: Although the IRB can suspend the research study, only the Institutional Official (VPAA) has the authority to suspend an individual's privileges to conduct research.

IRB Review of Corrective Action Plans:

As part of the noncompliance report to the IRB, investigators are required to outline a corrective action plan to prevent similar errors from occurring in the future. The IRB reviews this for adequacy and may require revision if not found to be sufficiently robust. Corrective action plans may include:

1. Additional education of the investigator and/or the research staff
2. Additional monitoring of support staff by the investigator, including more frequent staff meetings or review of work by an IRB committee member
3. Revisions to internal documents for processes

References:

Children's Hospital & Research Center, Oakland. Institutional Review Board Deviations Policy

Florida Hospital Institutional Review Board 212 E. Winter Park St. Orlando, FL 32804 (407) 303 5581; Fax (407) 303 3638 Deviations Policy and Procedure

NIH IRB Professional Administrators Committee, Version 5.1, Regulatory Process Workgroup

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