



Policy Name: – Protocol Deviation - Policy and Procedures			
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I. INTRODUCTION

Federal regulations require the IRB to review proposed changes in any research activity and to ensure that the investigator does not initiate such changes in approved research without IRB review and approval except when necessary to eliminate apparent immediate hazards/risks to the subject. Research activity includes all aspects of the conduct of the research study (e.g., recruitment methods, consent process, procedures used to protect privacy and confidentiality, etc.) and all of the information outlined in the IRB application/protocol reviewed and approved by the IRB. Most of these changes are submitted as amendments which undergo expedited or full committee review.

II. DEFINITIONS

A protocol deviation is any variance from the protocol involving a subject or subjects that is not approved by the IRB prior to its initiation or implementation, and occurs when a member of the study team departs from the IRB-approved protocol in any way **without the investigator first obtaining IRB approval.**

Deviations range in seriousness according to how the changes may impact subject safety, the degree of noncompliance with federal and state regulations, and the degree of foreknowledge of the event. Anticipated changes to a protocol should always be reported before the event occurrence unless an immediate change is necessary to protect subject safety. Note that repeated deviations of the same type may be an indication that an amendment is needed to permanently change study criteria.

Examples of deviations may include, but are not limited to:

- Failure to obtain informed consent, i.e., there is no documentation of informed consent, or informed consent is obtained after initiation of study procedures;
- Enrollment of a subject who did not meet all inclusion/exclusion criteria;
- Performing study procedure not approved by the IRB;
- Failure to report serious unanticipated problems/adverse events involving risks to subjects to the IRB and (if applicable) the sponsor;
- Failure to perform a required lab;
- Drug/study medication dispensing or dosing error regardless of whether a subject was negatively impacted;
- Study visit conducted outside of the time frame listed in the IRB-approved protocol;
- Failure to follow data and safety monitoring plan;
- Implementation of unapproved recruitment procedures;

- individual obtaining informed consent not listed on IRB approved study personnel list;
- Missing original signed and dated consent form (only a photocopy available);
 - Missing pages of executed consent form;
 - Inappropriate documentation of informed consent, including:
 - missing investigator signature;
 - copy not given to the person signing the form;
 - someone other than the subject dated the consent form;
 - initial's missing from each page – or from HIPAA privacy notice;
 - Use of invalid consent form, i.e., approved consent form without IRB approval stamp or outdated/expired consent form;

What are NOT considered to be protocol deviations?

Changes or departures from the study design or procedures that are due to a study participant's non-adherence are not considered to be protocol deviations and should not be submitted to the IRB. However, study participant non-adherence to the study design and/or procedures should be documented in the research records and should be reported to the IRB as an incident if the event adversely impacts the study participant's safety or well-being, or if a pattern of protocol departures indicate a need for changes in the protocol or informed consent document(s).

Examples:

- Study participant did not return for a scheduled study visit
- Participant refused a blood draw

A Single Patient /Subject Exception is when an investigator anticipates a one time, significant, time-sensitive intentional action or process that departs from an IRB approved protocol. In this situation he or she may request that a one time exception be granted by the IRB. The Principal Investigator may submit an amendment request for a one-time enrollment exception as a protocol modification request to the IRB. Obtaining prior approval for an enrollment exception modification avoids a protocol deviation. An enrollment exception request applies only to a single individual. Such a request should be rare and justified in terms of serving the best interests of the potential study participant. The enrollment exception amendment request will be referred to the appropriate Chair who will evaluate the level of IRB review required. An enrollment exception usually requires the additional approval of the study sponsor.

The IRB approval should note that this modification applies to one subject only and not to the study as a whole.

III. IRB NOTIFICATION OF PROTOCOL DEVIATIONS

The PI submits all protocol deviations that occur during the course of a study to the IRB immediately upon discovering them and no later than 10 working days following the discovery. The PI completes and submits the IRB Protocol Deviation Report Form. A corrective action plan must be submitted with the protocol deviation.

The PI also reports all protocol deviations to the sponsor, if applicable, following the sponsor's requirements. *Note:* The above definitions may not match the Sponsor's definition.

With one exception, regulations require prior IRB approval for proposed changes in the ongoing conduct of research studies. The one exception is when changes to the protocol are necessary to eliminate or reduce an apparent immediate hazard to the safety of research participants. Under this one exception, regulations allow changes to be initiated without prior IRB approval. However, please note that such changes must be reported to the IRB as an incident within 5 working days of initiating the changes in the study procedure(s). The incident report should consider whether an appropriate modification to the study application/protocol and/or consent document(s) is necessary.

IV. IRB AND OTHER INSTITUTIONAL RESPONSIBILITIES

IRB staff member screens the IRB Protocol Deviation Report Form for completeness and accuracy. If the submission is incomplete, IRB staff member requests additional information from the PI, which is returned to the IRB upon completion.

The IRB staff member sends the completed IRB Protocol Deviation Report Form with any applicable attachments to the IRB Chair or his/her designee.

The IRB Chair makes a determination regarding whether the deviation appears to meet the institutional definition of an Unanticipated Problem involving risk to participants or other and/or an instance of Serious or Continuing Noncompliance. If the deviation is minor, the IRB Chair or his/her designee conducts review using expedited procedures.

If the protocol deviation report undergoes Full Board review, the IRB Chair has the option to invite the investigator to attend the meeting to answer any questions or concerns that the IRB may have concerning the protocol deviation.

If the IRB determines that the deviation is reportable to external agencies, the IRB Chair will promptly notify the Institutional Official (IO) and submit a written report to the IO within 10 working days after review of the event by the convened Board. The Institutional Official will review the event and discuss the report with the IRB. The Institutional Official will notify OHRP, the FDA (if appropriate), the sponsor, and other agency officials as appropriate with 10 working days of receiving the Chair's report.

If the research study is a VA protocol, and the IRB determines the deviation is reportable to external agencies, the following will be notified: 1) The Associate Chief of Staff/Research & Development: 2) the VA Privacy Office (when the report involves unauthorized use, loss, or disclosure of individually identifiable patient information). VA policy for reporting to the VA Office of Research Oversight will be followed.

V. REFERENCES

- [45CFR46.103\(b\)\(4\)\(iii\)](#)
- [21CFR56.108\(a\)\(4\)](#)
- IRB Protocol Deviation Report Form