

Deviations in approved research – what should be reported, when and how?

Purpose:

This guideline provides information intended to clarify what events are considered deviations from approved research, what deviations need to be reported to the IRB, what information is needed by the IRB to review the deviation, and how the study team should provide that information in a timely manner to ensure compliance with current IRB policy. [See Washington University Institutional Review Board (IRB) policy and procedures document; section X.B.1]

Target Audience: Researchers, study coordinators, Human Research Protection Office (HRPO) staff, and IRB committee members.

• DEFINITIONS.

• Deviation

Any alteration or modification to the IRB-approved research without prospective IRB approval. The term *research* encompasses all IRB-approved materials and documents including the detailed protocol, myIRB application, consent form, recruitment materials, questionnaires/data collection forms, and any other information relating to the research study.

• Minor Deviation

A minor or administrative deviation is one that does not have the potential to negatively impact the rights, safety, or welfare of participants or others or the scientific validity of the study.

• Major Deviation

A major deviation is one that does have the potential to negatively impact the rights, safety, or welfare of participants or others or the scientific validity of the study.

• POLICY STATEMENT

Investigators are responsible for conducting human-subjects research in accordance with all applicable federal, state, and local laws and regulations as well as all Washington University policies including WU IRB policies and procedures. Federal regulations specifically require the IRB to review proposed changes in a research study, and to ensure that such changes in approved research are not initiated without IRB review and approval except when necessary to eliminate immediate hazards to the participant(s) or others [45CFR46.103(b)(4)(iii) and 21CFR56.108(a)(4)]. Planned changes to the IRB-approved protocol are to be submitted to the HRPO through use of the modification application and must be approved prior to initiation or implementation of the change.

- **Report What and When?**

- Major deviations

- Must be reported to the IRB within 10 working days of the occurrence of the event or notification to the Principal Investigator of the event. The only exception to this timeframe is a major deviation that results in the death of a WU/BJH/SLCH participant. Major deviations resulting in death must be reported within 1 working day of the occurrence of the event or the notification to the Principal Investigator of the event.
- Major deviations should be submitted using the REF application.
 - If the deviation represents an Unanticipated Problem or was made in response to an Unanticipated Problem, select “An unanticipated problem involving risks to participants or others...” as the REF application type.
 - If the deviation was not made in response to an Unanticipated Problem, select “Noncompliance” as the REF application type.

- Minor or Administrative Deviations

- Researchers are responsible for monitoring their studies throughout the year for adherence to the IRB approved protocol. The purpose of this monitoring is to identify major deviations and to look for trends in minor deviations that may indicate a systemic issue in how the study is being conducted that could potentially negatively impact the rights, safety, or welfare of participants or the study’s ability to produce scientifically valid results.
 - A series of minor deviations pointing toward a more global issue that could affect the rights, safety or welfare of the participant or affect the validity of the study should be reported as a major deviation.
 - In all other instances, a summary of minor deviations should be provided to the IRB at the time of continuing review, if the study will require continuing review.
 - The summary should be included in the continuing review application as part of the description of the overall study progress.
 - Do not submit a document that simply lists all of the deviations that occurred during the conduct of the study.
 - An example of an appropriate summary is as follows: “There were a few minor deviations that have occurred which included several out of window visits due to inclement weather or scheduling issues with the participants and 2 participants failed to bring their medication diary to a follow up visit. There were no systemic issues identified with these deviations.”

- **Examples**

The following examples are intended to be a guide to investigators and study team personnel. These lists are not all-inclusive.

- Major Deviations

- Failing to obtain legally effective consent prior to initiating research procedures. This includes failure to obtain signed consent when required.
- Medication errors, such as administering the wrong study drug to a participant or the wrong dose of the right study drug.
- Failing to conduct a study procedure or administer a study assessment that was meant to assess the safety of the individual's continuation in the study.
- Changes necessary to eliminate apparent immediate hazards to a participant or others.
- Informed consent obtained by someone other than individuals authorized by the IRB to obtain informed consent.
- Enrollment of a participant who did not meet all inclusion/exclusion criteria.
- Performing a study procedure that has not been approved by the IRB.
- Failure to report an Unanticipated Problem to the HRPO and/or sponsor of the study.
- Study visit conducted outside the required timeframe that, in the opinion of the investigator, may impact the safety of the participant.
- Failure to follow the IRB-approved safety monitoring plan.
- Implementation of recruitment procedures that have not been IRB-approved.

- Minor Deviations

- Receiving completed questionnaires back from participants where items are missing.
- Completing a study visit outside of the required timeframe when, in the opinion of the investigator, there are no safety implications.
- Use of an expired consent form in which the information contained is not substantively different than the currently approved consent, unless the deviation occurs repeatedly.
- Minimal over-enrollment
- A signed copy of the consent form was not given to the participant.

- Documentation deficiencies in the consent form such as:
 - A missing investigator signature
 - The participant signs the consent form but does not print their name in the signature block.

Note: A participant that does not sign and date the consent form prior to the initiation of research is considered a major deviation.

- **Points to remember**

- It is the responsibility of the Principal Investigator to determine whether an unapproved deviation is major or minor and to ensure proper reporting to the IRB. When making the determination of whether the unapproved deviation is major or minor, the Principal Investigator should consider whether the deviation negatively affected any of the following:
 - The rights, safety or welfare of the subject
 - The scientific validity of the study (the ability to draw conclusions from the study data)
- Please be aware that outside of the IRB reporting requirements you may be subject to other reporting requirements with the sponsor or FDA.
- For research conducted under ICH-GCP guidelines, HRPO interprets the reporting requirements outlined in this document to meet the reporting requirements of 4.5.2 which state:
 - For research conducted under ICH-GCP guidelines: ICH 4.5.2 states that “an investigator should not implement any deviation from, or changes of, the protocol without agreement by the sponsor and prior review and documented approval/favorable opinion from the IRB/IEC of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial (e.g., change of monitor(s), change of telephone number(s)).