Guidance for Reporting Research Events and Noncompliance

Investigators are expected to be familiar with and comply fully with the reporting requirements as specified in *Policy 801 Reporting Research Events* and with the requirements specified *Policy 802 Non-compliance in Human Subjects Research*.

This guidance document is intended to provide additional information that may be helpful to the investigator in interpreting these policy documents. However, this guidance does not supersede any requirements specified in the policies.

Main points

1. Reportable events requiring expedited reporting should be submitted in PROTECT using the Reportable New Information (RNI) form. Events that require expedited reporting are described in *Policy 801 Reporting Research Events* and include:
    - Major protocol deviations
    - Noncompliance that is not a protocol deviation
    - Unanticipated problems
    - New information that might affect the willingness of a subject to enroll or remain in the study
    - Death of a participant that are at least possibly related to research
    - Subject complaint that cannot be resolved by the study team
    - Use of a short form consent process
    - Audit, inspection or inquiry by a federal agency
    - Any FDA Form 483 issued regarding an NIH research protocol
    - Receipt of Sponsor notification that the IND for the protocol has been withdrawn
    - Breach of confidentiality/PII breach
    - Change to the protocol taken without IRB review to eliminate an apparent immediate hazard to a participant
    - Incarceration of participant in a study not approved by the IRB to enroll prisoners
    - Premature suspension or termination of research by the sponsor, investigator or institution
2. All reportable events, except for deaths, must be reported within 7 calendar days.
3. Deaths that are at least possibly related to research must be reported within 24 hours.
4. If an event is a protocol deviation, investigators should consider whether a protocol deviation is minor or major. Only major protocol deviations need to be reported in an expedited manner.
5. Noncompliance that is not a protocol deviation should be reported in an expedited manner. For example, failure to encrypt an email that includes study participant PII is noncompliance with NIH Policy and requires expedited reporting.
6. Reporting at the time of continuing review should consist of a summary description of all deviations (including noncompliance that is not a protocol deviation) as well as a description of any AEs and SAEs that have taken place at a greater frequency or severity than expected. Refer to the checklist on the Continuing Review Smart Form in the PROTECT electronic IRB (eIRB) system.

Deviations in approved research – what should be reported to the NIH IRB, when and how?

Protocol Deviation (PD) - Any change, divergence, or departure from the IRB-approved research protocol.

Major Deviations - Deviations from the IRB approved protocol that have, or may have the potential to, negatively impact, the rights, welfare, or safety of the subject, or to substantially negatively impact the scientific integrity or validity of the study.

Minor Deviations - Deviations that do not have the potential to negatively impact the rights, safety, or welfare of subjects or others, or the scientific integrity or validity of the study.

Report What and When?

Major deviations: A major deviation must be reported within 7 calendar days of an investigator becoming aware of an actual or suspected deviation.

- Major deviations resulting in death must be reported within 24 hours of the occurrence of the event or of any member of the study team becoming aware of the death.

Minor 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 that occurred since the prior Continuing Review should be provided to the IRB at the time of continuing review consistent with requirements on the Continuing Review Smart Form.

An example of an appropriate summary is as follows: "There were a total of 10 deviations that have occurred which included 8 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 obtained 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.
- Enrollment of a participant who did not meet all inclusion/exclusion criteria.
- Performing a research procedure that has not been approved by the IRB.
- Failure to report an Unanticipated Problem to IRB 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.

Minor Deviations

- Receiving completed questionnaires back from participants with some uncompleted items.
- 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 who 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 a deviation is major or minor and to ensure proper reporting. 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, investigators may be subject to other reporting requirements with the sponsor or FDA.

Noncompliance

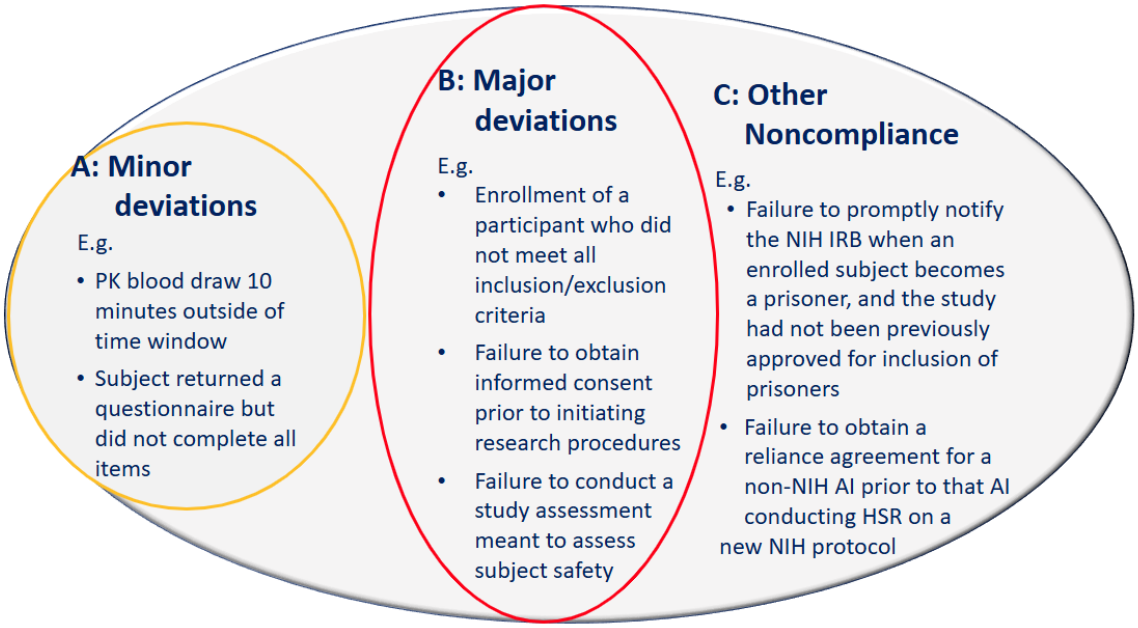
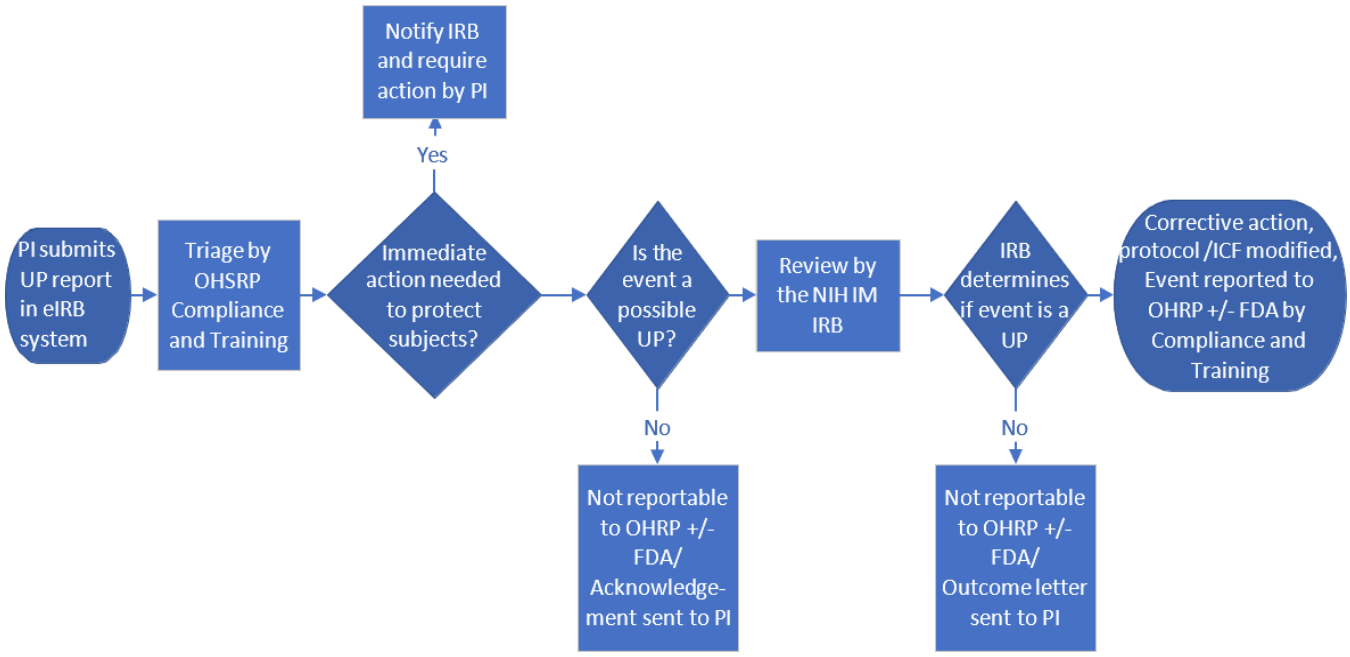


Diagram of relationships of non-Compliance and protocol deviations:

- Events in A + B + C represent noncompliance
- Only B and C need to be reported to the NIH IRB within 7 calendar days
- Events in A can be reported at Continuing Review (as part of a high-level summary of all deviations)

Flow chart for how possible unanticipated problems are evaluated



Flow chart for how events that constitute possible noncompliance will be evaluated