Quick Reference Guide

Reportable Events (Potential Unanticipated Problems and Protocol Deviations)

This Quick Guide is a supplement to ***INVESTIGATOR GUIDANCE: Unanticipated Problems and Adverse Events, INVESTIGATOR GUIDANCE: Protocol Deviations,*** *and* ***HRP-112 SOP: New Information****.*

1. When do I need to report Adverse Events to the IRB?

An Adverse Event (AE) only needs to be reported to the IRB as a potential Unanticipated Problem (UP) if the PI believes the event meets **ALL** of the following criteria:

- Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- Related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Adverse events that do not meet these criteria must be summarized at Continuing Review and reported on the Annual Event Summary form. Minimal risk studies are excepted from this requirement.

Potential UPs that must be reported fall into four categories:

Category #1

Must fit all 4:

1. On Protocol
2. Serious Adverse Event
3. Unanticipated
4. Related or Possibly related

Category #2

Must fit all 4:

1. On Protocol
2. Anticipated AE or SAE
3. Related or Possibly related
4. Occurring at a higher frequency or severity

Category #3

Must fit all 3:

1. Unanticipated AE or SAE
2. Related or Possibly related
3. May alter the risks and therefore warrants changes to the protocol, DSMP, or consent process

Category #4

Must fit all 3:

1. Unanticipated
2. "Other" events
3. May place subjects or others at a greater risk of harm or discomfort. Harm need not have occurred.

Timelines for reporting to the IRB:

- **7 calendar days:** Deaths and potentially life-threatening events that meet the definition of a potential UP
- **15 calendar days:** All other potential UPs

2. When do I need to report Protocol Deviations to the IRB?

In general, Protocol Deviations (PDs) must be reported if (1) they have the potential to adversely affect the rights or welfare of subjects; (2) they represent a pattern of noncompliance that is likely to continue without intervention; or (3) they represent recurrence of an issue following a requirement of corrective action by the IRB.

Timelines for reporting to the IRB: Within **10 business days** of discovery, except that deviations involving serious harm or risk of harm must be reported within **24 hours**.

To facilitate reporting, the IRB delineates three levels of PDs: Minor, Moderate, and Major. Moderate and Major deviations must be reported. Minor deviations do not need to be reported unless they represent a pattern of noncompliance. Examples of each category are described below:

Category	Harm/Risk of Harm		Administrative
Minor *no need to report unless multiple instances*	☐ The deviation resulted in no harm or risk of harm to research participants; or ☐ The deviation did not result in or require any substantive action to be taken or result in a substantive change to the subject's condition or status (i.e., did not affect the subject's participation in a substantive way, did not result in a change to the subject's emotional or clinical condition, did not cause an adverse experience or require a change to the clinical care of the subject, etc.)	**and/or**	☐ The deviation had no substantive effect on the value of the data collected (i.e., the deviation does not confound the scientific analysis of the results); or ☐ The deviation did not result from willful or knowing misconduct on the part of the investigator(s); or ☐ The deviation is easily corrected (e.g., consenting a subject with an old version of an ICF, recording data on an expired/incorrect form, forgetting to record data that may be acceptably recorded at the next visit, etc.)
Moderate *report to IRB*	☐ The deviation resulted in a harm or risk of harm that is not significant; or ☐ The deviation resulted in the need for minimal risk interventions, such as those defined in 45CFR46.110 and 21CFR56.110;	**and/or**	☐ The deviation resulted in the loss or improper collection or recording of some data for one or more subjects, but did not invalidate the entire data set for the study; or ☐ The deviation resulted in a regulatory violation that can be acceptably resolved; or ☐ Repeated minor protocol deviations from the same laboratory, site or research team; or ☐ There has been a failure to follow action ordered to correct minor or moderate protocol deviations
Major *report to IRB*	☐ The deviation resulted in or required a substantive action to be taken or resulted in a change to the subject's condition or status; ☐ The deviation has significantly harmed or posed a risk of significant harm to research participants;	**and/or**	☐ The deviation has substantially damaged the scientific integrity of the data collected for the entire study; ☐ The deviation is evidence of willful or knowing misconduct on the part of the investigator(s); ☐ The deviation involves serious or continuing noncompliance with federal, state, or local research regulations; ☐ There have been repeated minor and/or moderate protocol deviations from the same laboratory, site or research team; ☐ There has been a failure to follow action ordered to correct minor and/or moderate protocol deviations; or ☐ There has been a failure to follow action ordered in accordance with the emergency action provision of this policy

3. What happens after the IRB receives a UP or PD report?

The IRB follows **HRP-112 SOP: New Information** in reviewing your report in order to determine whether the event represents an Unanticipated Problem and/or Serious or Continuing Noncompliance. You will receive a memo detailing the IRB's determination and any corrective actions the IRB requires.

If the IRB determines that the event is an Unanticipated Problem and/or Serious or Continuing Noncompliance:

- The IRB will review the event at a convened meeting, along with any corrective and preventative actions you have proposed (including a modification to your study if you have submitted one), and determine whether any further actions are needed in order to protect subjects.
- The IRB office may be required to report the event to the federal authorities that regulate your study, such as the FDA or the Office for Human Research Protections (OHRP). The IRB will also report certain events to institutional authorities as required by IRB policy.
- You are responsible for reporting the event to sponsors/funding agencies as required by your protocol, and if you are the IND or IDE holder, to the FDA as required by the applicable regulations (see **HRP-815 INVESTIGATOR GUIDANCE: Additional FDA Obligations**).