Office of Human Research Protection
Institutional Review Board
701 Grove Rd
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Greenville, SC 29605

GUIDANCE – Reportable Event Submission Timing

Protocol Deviations	• Promptly: if substantive deviation from protocol and affects rights, safety or welfare of subjects, their willingness to continue in study or the integrity of the research data. • Periodically: if they do not affect any of the above.
SAEs, AEs, or Deaths	• Promptly: SAEs/AEs that represent an *unanticipated problem (UP)* or related deaths. • Periodically: if the SAE/AE is expected and related to study participation or unrelated deaths. • Never: SAEs/AEs if not related to study participation.
Confidentiality Breach	• Always promptly reportable to the IRB.
Non-Compliance	• Always promptly reportable to the IRB. The applicable Full Board IRB committee will review if event is possibly serious and/or continuing.
External IRB	• Submit the reportable event to the external IRB in their required timeframe and by their reporting guidelines. • Promptly submit internal related deaths & periodically submit aggregate reportable events list to Prisma Health IRB. • Egregious events should be reported to both the reviewing and the Prisma Health IRB.

Promptly: 10 business days from the date the PI first learned about the event | **Periodically**: at continuing review |**Unanticipated Problem**: event that is unanticipated, related and involving risk to participant or serious.

DEFINITIONS

Substantive Protocol Deviations:
The following deviations are considered substantive and are always reportable to the IRB:

- Deviations involving errors during eligibility process that caused the enrollment of an ineligible subject
- Missed protocol-required labs or procedures indicated before study intervention, including pregnancy tests (even if harm did not occur)
- REMS requirements deviations
- Drug dosing errors involving safety concerns (for example, if a subject was dosed incorrectly at a lower or higher dose, or if the drug was not stored per manufacturer indications)
- Consent process errors (when subjects did not receive an adequate explanation of study, or there is no correct documentation of consent)
- Any other egregious protocol deviation considered significant by the sponsor or PI

Unanticipated Problem (UP):
Any unanticipated problem related to the research, whether serious or not, that adversely affects the safety, rights, or welfare of subjects or others.
Generally, a UP is an event that satisfies all three following criteria:

1. Related to the research study itself;
2. Unanticipated (unexpected, not described in study docs, or higher frequency/severity); AND
3. Adversely affects the safety, rights, or welfare of subjects or others.

Breaches of confidentiality are to be considered as unexpected even if they are described in the ICF.

Serious Noncompliance (SNC)[1]
Noncompliance which, in the judgment of the convened IRB, significantly increases risk to participants, significantly decreases potential benefits, or compromises the integrity of the Human Research Protection Program (HRPP).

- The IRB does not have to find that harm has occurred, or was likely to occur, to make a determination of serious noncompliance.
- Multiple instances of noncompliance that are deemed not-serious individually may constitute serious noncompliance when considered collectively.

- The Board may consider mitigating factors, such as corrective action, that play a role in the determination of whether the event increased risk, decreased potential benefits, or negatively affected the integrity of the HRPP, but if despite these factors, the event's occurrence meets the definition of serious noncompliance, and then the event should be categorized as such.

Continuing Noncompliance (CNC):
A pattern of non-compliance that indicates a lack of understanding or disregard for the regulations or institutional requirements that protect the rights and welfare of participants and others, compromises the scientific integrity of a study such that important conclusions can no longer be reached, suggests a likelihood that non-compliance will continue without intervention, or involves frequent instances of minor non- compliance. Continuing non-compliance may also include failure to respond to a request from the IRB to resolve an episode of non-compliance or a pattern of minor non-compliance.

OHRP has advised that it considers noncompliance to be continuing if it persists after the investigator knew or should have known about it. In such cases, the Prisma Health IRB holds a presumption of continuing noncompliance, placing the burden on the investigator to present compelling, mitigating circumstances. The period in which the continuing noncompliance occurred could be days or weeks (depending on the seriousness of the matter), and the IRB does not need to call an issue noncompliance before being able to call it continuing noncompliance.[2]

Prompt vs. Periodic reporting: Prompt reporting is reporting done with a reportable event form that should occur within 10 business days of event occurrence, or from when the PI first learned about the event. Periodic reporting is reporting done with a summary at the time of continuing review.

Internal vs. External events: An internal event is an event occurring to a subject who was enrolled at Prisma Health or at a site in which the Prisma Health IRB is the IRB of record. For example, if a subject enrolled at Prisma Health experienced an event at a different medical facility, the event will still be considered an *internal* event. In addition, if another site relied on the Prisma Health IRB for review (through a reliance agreement), that site will be considered *internal*.

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[1] The U.S. Office of Human Research Protections (OHRP) has advised IRB that it considers the following always to be serious noncompliance:
- Human subjects research conducted without IRB approval
- Substantive change to the research implemented without IRB approval

[2] Borror, Kristina. *Guidance on Reporting Incidents to OHRP*. Webinar accessible at http://videocast.nih.gov/launch.asp?18537