GUIDANCE: Reportable New Information (RNI) Reporting

Research regulation and the ethical principles at its core mandate that human subjects research be well-designed and well-executed with an obligation to minimize risks to participants within the approved protocol. To achieve this, the PPHS expects that researchers will strive to continually monitor their research and identify issues that may impact care. This is a proactive requirement and should take place whether or not there was an actual harm and independently of the need to report promptly or in aggregate at the time of continuing review to the PPHS.

Just as reporting to the IRB/PPHS does not eliminate the need for a Data Safety Monitoring Plan that may include a formal DSMB/C, the obligatory reporting of issues to the PPHS does not eliminate the need for continual monitoring by the PI and team. There are a variety of effective ways to monitor human participants' safety in research and the monitoring should be commensurate with the level of research risk. The monitoring plan should be included in the protocol/HRP-503 and may include internal monitoring (e.g., PI review and departmental research quality programs) and/or external monitoring (e.g., sponsor/CRO audits). Exceptions to the reporting requirements highlighted below may be acceptable based on an IRB-approved individualized monitoring plan.

The following guidance provides information on ISMMS IRB's requirements for reporting new information for projects that rely on the ISMMS IRB. The instruction below is not a complete list of events that require reporting to the IRB. For a complete list of reporting categories, refer to the Investigator Manual, or the RUTH Reportable New Information (RNI) smart form.

If you are unsure about whether something meets the criteria, please contact the PPHS at IRB@mssm.edu. For studies relying on an external IRB, please see HRP 923-Guidance-RNI Reporting for R2Rs for further instruction.

Section I: General Reporting Considerations:

- Reporting may be required 1) in aggregate at the time of continuing review, 2) promptly, within five (5) business days of learning of the incident, and/or 3) immediately, within one (1) business day, as defined in this policy.
- Immediate (within one (1) business day) and prompt (within five (5) business days) reporting to the PPHS will be done through RUTH as an RNI.
- Aggregate reports at the time of continuing review should be attached to the Continuing Review submission in RUTH.
- Notices of suspensions or terminations require reporting within one (1) business day.
- In addition to the requirements outlined in Sections II and III, examples of incidents that

require prompt reporting (within five (5) business days):

- Any written report of study monitors, internal or external audit reports, DSMB reports.
- Any subject complaint that cannot be resolved by the research team.
- Incarceration of a subject in a study that has not previously been approved by the IRB under 45 CFR 46, Subpart C to involve prisoners.
- If an individual becomes pregnant in a study that has not been previously approved by the IRB under 45 CFR 46, Subpart B to enrolling pregnant individuals, must be reported to the IRB if the PI wishes to have the individual continue in the research.

- The IRB does not prospectively approve deviations that have not yet occurred. The expectation is that your protocol is formally amended via a modification submission if any changes are being proposed to your study. Do not submit an RNI asking the PPHS to approve a "waiver" or "exception" to a protocol. Immediate safety concerns should trigger a change to the protocol prior to PPHS review. Please contact the PPHS if there is a specific scenario to discuss.

Section II: Adverse Event Reporting:

- Report all ***unexpected and at least probably related adverse event(s)*** to the research procedures if, in the opinion of the investigator, the research procedures more likely than not caused the harm regardless of other reporting (i.e. reports to sponsor or outside entities). Reporting to the ISMMS IRB must occur within five (5) business days of learning of the event.
- Report all ***serious adverse event(s) at least probably related*** to the research procedures if, in the opinion of the investigator, the research procedures more likely than not caused the harm as defined below. Reporting to the ISMMS IRB must occur within one (1) business day of learning of the event. For more information on reporting serious adverse events, click here.
  - Death
  - Life-threatening
  - Hospitalization (initial or prolonged)
  - Disability or Permanent Damage
  - Congenital Anomaly/Birth Defect
  - Required Intervention to Prevent Permanent Impairment or Damage (Devices)
  - Any serious psychological and emotional distress resulting in study participation (suggesting need for professional counseling or intervention)
  - Other Serious (Important Medical Events) as determined by the PI
- If event(s) was expected and the research team has followed their monitoring plan and have reported the event to their DSMB or DMC, reporting an aggregate AE log to the ISMMS IRB occurs at the time of continuing review.

- If the event(s) was expected but during regular oversight the research team identified a higher rate of frequency or severity of said event(s), reporting to the ISMMS IRB must occur within five (5) days of that discovery.
- If the event(s) is not related to the research at all, do not report to the IRB even at the request of the sponsor or others. If the event(s) is not related, it is not reportable.

Section III: Non-Compliance/Failure to Follow the Protocol Reporting:

Researchers are reminded that they may not alter a protocol prior to IRB approval unless the change is needed to address an apparent immediate risk to participants. If this should occur, it should be reported to the PPHS within five (5) business days. More than likely, a formal protocol modification will be needed and should be submitted in a timely manner.

All instances of non-compliance are expected to be reported to the PPHS as an aggregate report at the time of the project's continuing review submission and should be attached to the continuing review submission. However, some instances require prompt (five (5) business day) reporting to the PPHS.

Exceptions to prompt reporting may be allowed if there is a documented plan to monitor the project which has been approved by the IRB that addresses the frequency of reporting.

The list below is intended to guide in your prompt reporting decision-making and is not all-inclusive. Examples may include:

- Failure to obtain legally-effective informed consent.
- Informed consent obtained after initiation of procedures for research purposes.
- Research projects conducted without prior IRB approval.
- Modifications to the protocol enacted prior to IRB approval.
- Continued study procedures after IRB approval has lapsed without first obtaining permission from the IRB.
- Medication dispensing or dosing error if medication is part of the study design, not just investigational agents.
- Missing or unreturned investigational devices.
- Study procedures performed on an ineligible participant.
- Failure to follow safety monitoring plan.
- Continuing research activities after loss of license, registration, or clinical privileges.
- Conducting or continuing research activities by staff who were not listed as study staff on the IRB application.
- Violations of confidentiality and privacy, including HIPAA violations. These may also need to be reported to the HIPAA Privacy Officer.

- Failure to perform a required protocol assessment (e.g. lab test, imaging, symptom checklists, etc.) that may affect participant rights, safety or welfare or may compromise the data integrity of the study, as determined by the principal investigator.
- Study visit conducted outside of required timeframe that, may affect participant rights, safety, welfare or may compromise the data integrity as determined by the principal investigator.
- A series of deviations in a single study or single patient that collectively, in the opinion of the principal investigator, would pose greater risk to patients or undermine the scientific integrity of the data.

PPHS wishes to emphasize that an event in the last three categories only needs prompt reporting if it had a reasonable possibility of impacting the rights, safety or welfare of study participants or may compromise the data integrity of the study. The reporting obligation is present even if no actual harm (includes physical, psychological, economic or social harm) occurred to a participant. The principal investigator is responsible for determining if the event meets the "reasonable possibility" threshold using best clinical judgement aligning with what other reasonable clinicians in the specialty of interest would conclude.

For example, an imaging study obtained a couple of weeks outside of the specified timeframe, or labs (when there is no expected toxicity or clinical suspicion) obtained past the data collection window would appropriately be reported to the PPHS at continuing review. In contrast, failure to perform procedures that are key to assessing for potential toxicity, as an example obtaining an echocardiogram within a reasonable window of pre-specified timeframe for a drug with potential cardiotoxicity, would be reportable to the PPHS promptly, within five (5) business days.

Noncompliance Reporting Requirements

- All noncompliance incidents are expected to be reported to the PPHS as an aggregate report at the time of the project's continuing review. The report will include noncompliance reported since the last IRB review as well as those that did not require prompt five (5) day reporting. *Note: The events that do not require prompt reporting are frequently referred to as "minor deviations." This is not a term used in this document as it is not defined in regulations and does not track with mandated reporting to OHRP and FDA*.

- A root cause analysis and corrective action plan will only be required for RNIs that may have a significant impact on the participant(s) rights, safety and/or welfare or may compromise the data integrity of the study, as noted above, and must be signed by the PI. In your plan, include information that is:
    - Specific: Identify the actions you or others will take to address the root cause
    - Timely: Include the date(s) when you or others will complete the actions.
    - Measurable: Include a process of assessing the action plan effectiveness and a process by which the plan will be amended if it is not effective.