Monday Morning Practice Pearls #17

What adverse events (AEs and SAEs) need to be reported to the IRB at the time of continuing review (CR) and what format needs to be used?

Revised August 2022

Per Office for Human Research Protections OHRP Continuing Review Guidance (2010), "One of the most important considerations for the IRB at the time of continuing review is whether there is any new information provided by the investigator, or otherwise available to the IRB, that would alter the IRB's previous conclusion that (1) the risks to subjects are minimized, and (2) the risks to subjects are reasonable in relation to anticipated benefits, if any, to the subjects and the importance of the knowledge that may reasonably be expected to result . . . The IRB's continuing review procedures should ensure that the IRB will consider relevant information received since the date of the last IRB review . . ."

Per NIH Policy 205 *Requirements for IRB Submissions*, "Required materials for Continuing Review (CR) of non-exempt human subjects research: . . . A high-level summary (not a line-item listing) of the following events that have occurred since the time of the last IRB IR or CR review, see Policy 3014-801 Reporting Research Events, e.g.: . . .Adverse Events and Serious Adverse Events that do not meet the definition of an Unanticipated problem (UP) . . ."

Per NIH Policy 801 *Reporting Research Events*, "Investigators must provide the following information to the IRB in summary format at the time of continuing review, or when otherwise specifically requested by the IRB or the OHSRP office of Compliance and Training. Investigators should provide a high-level summary of these events that have occurred since the time of the last IRB review and not a line-item listing. Adverse Events and Serious Adverse Events that do not meet the definition of an UP."

At time of CR, please provide the following information:

SAE

1. Total number of SAEs – specify:
    a. Number **related** to research
        i. For each event, use the specific CTCAE terms for summary (not system organ class) and include grade; describe if expected/unexpected per PI assessment, had any impact on risk profile
    b. Indicate if all events were treated and resolved
2. If the protocol has more than one phase or arm with different treatment regimens, summarize SAEs for each phase or arm separately.
3. If no SAEs occurred during the reporting period, please indicate this.
4. PI assessment of all events and if the events are within the frequency, severity and causality expected for the study. Also indicate If there is an impact on the risk profile of the study.

AE

1. Total number of AEs – specify:
    a. Number **related** to research
        i. Number Grade 1 or 2 –describe if they were expected/unexpected per PI assessment
        ii. Number Grade 3 or 4 – use the specific CTCAE terms for summary (not system organ class); describe if there were expected/unexpected per PI assessment, had any impact on the risk profile.
2. If the protocol has more than one phase or arm with different treatment regimens, summarize AES for each phase or arm separately
3. If no AEs occurred during the reporting period, please indicate this
4. PI assessment of all AEs and if the events are within the frequency, severity and causality. If there is an impact on the risk profile.

Example:

During the reporting period, there were a total of 5 serious adverse events, 3 were related to the research: 1- grade 2;-hematuria, 1- grade 3; anemia and I- grade 3; myocarditis. All SAEs were expected, treated and resolved.

There were 55 adverse events since the last continuing review and 43 were related to research and expected for research intervention. "G" indicates CTCAE grade: There were 6 anemia G2-3; 4 chest pain/cardiac G2; 3 ventricular tachycardia G2; 8 nausea G2-3; 4 diarrhea G2-3; 2 vomiting G2; 2 ALT increase G3; 2 AST increase G2; 4 CPK increase G3; 1 lipase increase G2; 5 papulopustular rash G2. PI reviewed and assessed all the SAEs and AEs and they are within expected severity and frequency for this protocol.

IMPORTANT: If event(s) are **not** within the expected severity and frequency, provide a high-level summary of those events to include what the impact was on subjects, include the following:

- severity of the event/ grade level
- description of event
- arm of the study the event occurred on (if applicable)
- clinical treatment (if applicable) outcome/resolution of the event
- If the event(s) required a dose modification
- If the event(s) triggered stopping rules

NOTE: If there was an AE/SAE that met the definition of Unanticipated Problem (UP), please indicate that a UP was submitted and include the REF number. Give a very brief summary of the UP. Indicate if the protocol &/ the consent form were revised. If there were no UPs during the reporting period, please indicate this specifically.

For more information see NIH IRBO Tips and Tricks (updated August 2022)

Related M2P2s:

- #50: What are the new expedited IRB reporting requirements for "events" that happen during research?
- #51: What research "events" need to be reported at the time of continuing review?