Reporting Unanticipated Problems and Adverse Events

Procedures

A. Responsibilities

1. Principal Investigators - It is the PI’s responsibility to analyze and review all adverse events (AEs) and Unanticipated Problem (UPs) that occur in studies on which he/she is the PI, determine if an AE is a UP, determine the appropriate action to be taken in response to AEs and UPs, and appropriately report UPs to the IRB. In the case of an On Protocol event in a Non-OHSU subject, the determination of whether the AE represents a UP lies with the central monitor.

2. Institutional Review Board - It is the IRB’s responsibility to review the reports, determine if modifications are needed in response to the UP, and to report unanticipated problems to the Federalwide Assurance (FWA) signatory official, any supporting department or agency head, and OHRP for OHSU internal events, if not delegated to a central monitor.

3. Central Monitor - It is the Central Monitor’s responsibility to analyze and review applicable On Protocol events for Non-OHSU subjects and Off Protocol events using the same drug or agent, determine if the AEs are UPs, and report the UPs to the PI for subsequent reporting to the PI's IRB. If OHSU is serving as a coordinating center, then the PI of the coordinating center is responsible for this determination via an approved monitoring plan.

B. Reportable Adverse Event Analysis

1. In order for the PI (or the Central Monitor) to determine whether a particular AE is “unanticipated” and also considered reportable as a UP, the following should be taken into account:
   • The description of known or foreseeable adverse events and risks in the IRB-approved research protocol, any applicable investigator brochure, the current IRB-approved consent form, and other relevant sources of information.
   • Any underlying disease or conditions of the subject experiencing the adverse event.
   • A careful assessment of whether the adverse event is related or possibly related to the subject’s participation in the study.

2. The UP analysis charts and/or the UP Decision Tree should be used to help make this determination. The charts provide
guidance on determining when an event is expected and related as well as when to report events that occur outside of OHSU or on different protocols.

3. Any event that is rare in the absence of drug exposure, such as agranulocytosis, hepatic necrosis, or Stevens-Johnson syndrome is always an unanticipated problem.

C. When to Report
1. All UPs, including AEs that meet the definition of a UP as determined by the PI or the Central Monitor, unless otherwise determined by the reviewing IRB, must be reported by the PI to the IRB as soon as possible, and within the following time frames:
   • Deaths and potentially life-threatening events must be reported within seven (7) calendar days after the PI learns of the event. If any of these SAEs requires a change (as determined by the PI or the IRB) to the protocol or consent form, the PI must make those changes promptly and submit the revised documents to the OHSU IRB.
   • All other UPs must be reported within fifteen (15) calendar days. If the event requires changes (as determined by the PI or the IRB) to the protocol or consent form, the PI must make those changes promptly and submit the revised documents to the IRB.

2. A brief summary of UPs as well as a brief summary of all adverse events must be submitted with the continuing review using the IRB template “Annual Event Summary” Form located on the IRB website.

3. The IRB reserves the right to request a report or additional information at any time.

D. How to Report
1. Reports are made through the eIRB, which will ask for the following information.

2. Reports of UPs, including AEs that meet the definition of an UP, must include the following information:
   • Study Information: Title, PI, IRB#, Sponsor/award #, IND/IDE#
   • Number of subjects enrolled to date and currently actively involved in research procedures.
   • Date of UP, Date notified of UP
   • Classification of the Experience Type: On protocol UP for OHSU Subjects, On protocol UP for Non-OHSU subjects, Off protocol UP (using same drug or agent), or Other Unanticipated Problem
   • Participant ID, if applicable
• Description of event
• Agent involved if applicable (for example, drug, device, placebo)
• Relationship of the agent or research procedures to the UP.
• Basis for UP determination: Analysis as to why the event represents a “problem” for the study and why it is “unanticipated”. For instances of increased frequency or severity, it must state how the frequency or severity diverges from the expected.
• Response Plan. Description of proposed actions, including modifications, to be taken by investigators in response to the UP

E. IRB Review of Submitted Unanticipated Problems

1. The IRB chairperson and/or designee will review the UP report and the response plan, including any proposed modifications, and triage it appropriately.
   • Proposed modifications which represent minor changes may be triaged for expedited review.
   • In the case of proposed modifications which represent more than a minor change or are otherwise not approvable under expedited review procedures, review will be referred to the full board for review and further action.
   • In all cases, the IRB Chairs reserve the right to refer any report or proposal to the full board.

2. If the response plan indicates that no modifications are proposed and the reviewer(s) agree, the report will be approved and no further action is needed.

3. If the reviewers believe that modifications are needed, either because no modifications were proposed in the response plan or because insufficient or incorrect modifications were proposed, the IRB chairperson will request in writing that the PI discuss this with the central monitor, if applicable, and submit a response or the necessary modification(s). In situations where there is not a central monitor, the PI will be required to respond.

4. All reports of UPs will continue through appropriate IRB review procedures until the reports and any applicable modifications are approved or disapproved. As with any disapproval, the PI may appeal the decision.

5. The IRB has authority to require submission of more detailed contextual information by the PI, sponsor, and study coordinating center or DSMB/DMC about any adverse event or unanticipated problem.
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