Revised AE-UP Reporting Module

The Adverse Event-Unanticipated Problem (AE-UP) Reporting Module has been revised to reduce the reporting burden for investigators by narrowing the scope of reportable events/problems, and to capture those events that could potentially be unanticipated problems involving risk to subjects or others. Events that are considered to be unanticipated problems must be reported to the IRB, appropriate UCI officials, the funding agency or study sponsor, and federal department or agency heads including the Office of Human Research Protections (OHRP), the Food and Drug Administration (FDA), when applicable.

What Needs to be Reported?

Lead Researchers are to report any unexpected, internal adverse events or external adverse events that occur anytime during the conduct of the research study or during the follow-up period after the research, which in the opinion of the UCI Investigator includes the following components:

- **Unexpected**, in terms of nature, severity, or frequency, given (a) the research procedures that are described in the IRB-approved documents, such as the protocol and informed consent document; and (b) the characteristics of the subject population being studied;

- **Related** or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or problem may have been caused by the procedures involved in the research); and

- **Suggests** that the research places subjects at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

While all events and problems should be reported to a study sponsor, not all events need to be reported to the IRB. For instance, expected adverse events and protocol deviations do not need to be reported to the IRB.

New Reporting Timeframes

Most reportable events and problems are to be reported within 10 working days; however, internal serious adverse events, protocol violations, changes to the protocol without prior IRB approval to eliminate an apparent immediate hazard to a research subject, and other events/problems involving subjects or others that are unexpected, related or possibly related to the research, and caused harm to others or places others at a greater risk of harm as a result of the research, must be reported to the IRB within 5 working days.

For detailed information about report timeframes and a complete list of reportable events and problems, see the [AE-UP webpage](http://www.rgs.uci.edu/ora/) and [AE-UP reporting module](http://www.rgs.uci.edu/ora/).
Except for human research studies that have been granted Exempt registration, DHHS and FDA regulations require the IRB to continually review ongoing research at intervals appropriate to the potential risk to participants, but at least annually.

While initial IRB review is based on the researcher’s best assessment of the anticipated benefits, risk, and procedures, the continuing review process is important because it is based on the conduct of the study. Actual risk can be evaluated and preliminary results can be used to assess the risk/benefit ratio. Additionally, the risk/benefit ratio may change not only because of unexpected results and effects of the research intervention itself, but because new knowledge resulting from related research may affect the balance.

Taking the time to provide detailed information requested on the form will prevent delays in continuing review and approval of the study. It is important to be responsive to the questions on the continuing review application so that the IRB can conduct a meaningful and thorough review.

Prepare the submission 90 days in advance for full committee protocols; 60 days in advance for expedited protocols:

1. Consider subject accrual, study progress and the informed consent process. Were there any problems with obtaining informed consent? Any subject withdrawals? Do modifications to the recruitment or consenting process need to be made?

2. Review any unanticipated problems and adverse events that have been reported to the IRB. Are there any events that should be considered at the time of continuing review? Based on the Lead Researcher’s assessment of expected and unexpected events, has the frequency or seriousness of the expected risks been greater than expected?

3. Multi-center studies: Is there any additional information from the Sponsor or Coordinating Center that should be reported to the IRB? Be sure to provide any data safety monitoring reports and/or interim reports from sponsors and coordinating centers.

4. Reassess investigator financial interests. Has any study team member’s financial interests in the study changed in the last year? See the COI disclosure requirements for more information.

5. Review all modifications/amendments to the study over the last year. Determine if additional modifications need to be submitted for IRB review and approval.

6. Review the risks and benefits of the study. Has there been a change in the risk/benefit profile? Take into account information gathered during the past year such as interim results, reportable events/problems, and/or changes in scientific knowledge.

Submit the continuing application 60 days in advance (for full committee protocols); 30-45 days in advance (for expedited protocols). Please do not submit continuing protocol applications any earlier than these suggested timeframes.

**Importance of Avoiding Lapses in Approval**

Protocol lapses can be detrimental to a research design and may impact subject safety and welfare. The IRB sends reminder emails to Lead Researchers, Faculty Sponsors (when applicable) and Administrative Contacts to assist with continuing application submission planning and to avoid lapses in approval. The e-mail reminder is sent 90 days prior to the expiration date for full committee studies and 60 days prior to expiration for expedited studies. A final reminder is sent 30 days before protocol expiration, followed by an expiration memo.

**What happens if there is a lapse in IRB approval?**

If the IRB has not approved a research study by the study expiration date, the protocol expires and all research activities must stop. This includes: recruitment and informed consent procedures; collection of data/information from or about living individuals; all research-related interventions or interactions with currently enrolled subjects; and analyses involving identifiable human subjects data.

*Exception:* when lapses are unavoidable, research-related interventions or interactions with enrolled subjects may continue if the IRB determines that stopping the research would jeopardize the rights or welfare of current subjects. Upon protocol expiration the Lead Researcher must submit by email a coded list of research subjects for whom expiration of the research would cause harm and what interventions may occur during the lapse.

The IRB Chair will review the list and allow individual participants to continue participating in the research interventions or interactions only when it is determined that it is in their best interest to continue. However, any information collected during the lapse in approval may not be used for research.