

Reportable Events

The University of Rochester (UR) has established an electronic reporting system for events that need to be reported to the Research Subjects Review Board (RSRB). The categories defined below are drawn from the federal regulations for the protection of research subjects (21 CFR 50/56 and 45 CFR 46).

It is important to know that some “events” are reportable to institutional review boards (IRB) and some are not. The Food and Drug Administration (FDA) has published guidance on Adverse Event reports, which may be accessed at <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126572.pdf>. The Department of Health and Human Services (HHS) has also published guidance on the topic of reporting to IRBs. Their guidance can be accessed at: <http://www.hhs.gov/ohrp/policy/AdvEvtGuid.pdf>. Additional assistance can be obtained from your RSRB Specialist (275-2388).

The FDA guidance states, “In the years since the IRB and IND regulations issued, changes in the conduct of clinical trials (e.g., increased use of multi-center studies, international trials) have complicated the reporting pathways for adverse event information described in the regulations. In particular, the practice of local investigators reporting individual, unanalyzed events to IRBs, including reports of events from other study sites that the investigator receives from the sponsor of a multi-center study—often with limited information and no explanation of how the event represents an unanticipated problem—has led to the submission of large numbers of reports to IRBs that are uninformative. IRBs have expressed concern that the way in which investigators and sponsors of IND studies typically interpret the regulatory requirement to inform IRBs of all “unanticipated problems” does not yield information about adverse events that is useful to IRBs and thus hinders their ability to ensure the protection of human subjects.”

The HHS guidance states that “only a small subset of adverse events occurring in human subjects participating in research are unanticipated problems that must be reported under 45 CFR part 46. The guidance is intended to help ensure that the review and reporting of unanticipated problems and adverse events occur in a timely, meaningful way so that human subjects can be better protected from avoidable harms while reducing unnecessary burden.”

If an event is not “**serious**” and “**unexpected**” and “**related**,” it does not need to be reported to the RSRB and, in fact, the system will not accept such reports. Related events that are not serious or not unexpected will continue to be accepted in the system, but are not reviewed until the continuing review for that study. If an investigator believes that a pattern of events is developing which was not expected, then a report under “unanticipated problems” (type 4) should be made.

Reportable Event Definitions:

“**Unexpected**” means that the event was unforeseen and has not been previously encountered, known, or recognized and was not identified in nature, severity, or degree of incidence in the protocol (investigational plan), supporting documentation, the informed consent document, or the RSRB application.

“**Unanticipated**” is interchangeable with “unexpected.”

“**Serious**” means (per FDA regulations 21CFR312.32) an event that results in any of the following outcomes: death, a life-threatening event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect, or requires medical or surgical intervention to prevent one of these outcomes. For non-FDA regulated studies “serious” means any event that causes a prolonged or permanent harm that is psychological, social, legal or financial.

“**Caused by**” means there is a causal association that can be attributed to the study.

“**Related to the study**” means that there is some aspect of the study (e.g., a research procedure, existence of a laptop database, etc.) that is directly related to the event (e.g., physical harm, breach of confidentiality, etc.).

“**Involving risks to subjects or others**” means some harm (physical, psychological, social, financial, or legal) or discomfort has occurred or is possible and affects subjects or “others” (e.g., subject’s family, research team, third parties, etc.).

Types of Reportable Events in the UR system:

Type 1: Locally occurring drug and medical device “adverse events” (reports of toxicity) per FDA definitions. There are reports of adverse events that occur at UR facilities or at sites for which the UR-investigator has responsibility.

Type 2: A batched report of several off-site adverse event reports with no study changes (amendments) requested. Sponsors (industry or federal) may send reports of adverse events occurring at any research or clinical site to investigators. While the RSRB accepts these because of sponsor requirements for investigators, there is no regulatory requirement to forward these to the RSRB. [NOTE: please check with your sponsor to determine if your contract/agreement requires such reports to be forwarded.]

Type 3: Is currently reserved for future use.

Type 4: An unanticipated problem involving risks to subjects or others (UPIRTSO) that occurs in a UR study or that impacts UR study subjects or the conduct of the UR study. Unanticipated problems involving risks to subjects or others (UPIRTSO) may or may not

be an “adverse event” per FDA regulations; report “non-toxicity” events as UPIRTSOs. Examples include a lost laptop with identifiable data, recruitment letters sent to the wrong people breaching privacy, accidental overdoses without toxicity, etc. [Note, if an amendment is needed as a result of the UPIRTSO, file the amendment instead of a reportable event report; the reason for the amendment will be the reportable event description.]

Type 5: Monitoring body reports (Data Safety Monitoring Board – DSMB, Data Monitoring Committee – DMC). Formal monitoring bodies send to investigators summary reports on the status of studies (e.g., keep open, close early, make study changes, etc.). These reports are reviewed when submitted and also in continuing review.

Type 6: New information (including changes in risks or benefits) that may impact the willingness of subjects to participate or continue to participate in the research study. New information of this type may come from the published results of other research studies, case reports, etc. as well as experience with the UR study or studies that the investigator is conducting. [Note, if an amendment is needed, e.g., to change the consent process/form, file the amendment instead of a reportable event report; the reason for the amendment will be the new information description.]

Type 7: Changes made to the research without prior RSRB approval in order to eliminate apparent immediate harm. This type of report should be used to report one-time changes that do not call for permanent changes (amendments) to the study. [Note, if an amendment is needed, file the amendment instead of a reportable event report; the reason for the amendment will be the reportable event description.]

Type 8: An incident of non-compliance with the University’s policies or the requirements or determinations of the RSRB. This type of report should be used to self-report non-compliance with federal regulations (e.g., an instance of not obtaining consent) or the requirements of the RSRB (e.g., not following recruitment procedures) that affect the rights, safety, or welfare of subjects or others.

Type 9: Investigator-initiated voluntary suspension of research. Investigators may suspend all or part (enrollment, test procedures, etc) of a research study to consider changes to the research, investigate risks to subjects or others, etc. These reports keep the RSRB apprised of the status of approved research. [Note, request for closure (termination) of a study is made by submitting a final continuing review report.]