



Regulation: There are plenty of regulations requiring that Unanticipated Problem Involving Risk to Subjects or Others (UPIRTSO) must be reported.

RISKS	Define them ahead of time. Plan.
RECOGNIZE	Look for them. If you don't look, you won't see.
RESOLVE	Treat the subject
REPORT	Record and report about each one either immediately or later
REVIEW	Examine the reports for trends
RECONCILE	Evaluate them in terms of expectations especially of frequency
RESPOND	Consider changing something
REPAIR	Prevent future recurrences
RESTITUTION	Make sure the subject isn't paying the price for being your research subject

What is a Problem? (Do not report)

We generally can recognize problems as they occur daily. Most problems are anticipated; we have trained for them and have procedures to deal with them.

- The computer froze and the data was lost but there was a back-up
- The surveys to be administered are still back at the office.
- You or the subject arrived at the right time – on the wrong day .
- The subject had a headache and didn't show up. (also a deviation).

What is an Unanticipated Problem? (Report on IRC form 4.35)

This sub-set of problems is why we have skilled and experienced professionals. This is the surprise. There was no mention of it in the protocol, the description of the previous studies. There is no plan in place.

- The completed surveys were left at the coffee shop
- The laptop was stolen
- The question that seemed innocuous caused a response.
- An interviewer at a subject's home was raped.

What is an Unanticipated Problem Involving Risk to Subjects? (Report on IRC form 4.35)

Did the authors mean risk of harm or actual harm? Report both. In this area we incorporate a seriousness (not trivial but enough to require action or medication or costs to subject or investigator) and relatedness. Relatedness might not be clear until it happens again or until a trend emerges. Harms can be physical, legal, social, emotional or financial (loss of insurability).

- The laptop was stolen and it had identifiable sensitive information.
- The question that seemed innocuous caused hysterical sobbing.
- Taking a child from a classroom results in a student becoming seriously marginalized.
- It is determined that several subjects were incapacitated by the serious headache.

What is an Unanticipated Problem involving Risk to Others? (Report on IRC form 4.35)

Others is a big category including colleagues, current or future subjects and people relying on the results of the study.

- Other interviewers were at risk and are now sent out only in pairs.
- The database on the computer is of subjects and people who were on a contact list.



Definitions

312.66	An investigator shall assure that ... he or she will promptly report to the IRB ... all unanticipated problems involving risk to human subjects or others,
812.3(s)	<i>Unanticipated adverse device effect</i> means any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.
312.3	" <i>Associated with the use of the drug.</i> " There is a reasonable possibility that the experience may have been caused by the drug.
312.3	"Unexpected" as used in this definition refers to an adverse drug experience that has not been previously observed (e.g., included in the investigator brochure) rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product.
312.3	" <i>Unexpected adverse drug experience</i> " Any adverse drug experience the specificity or severity of which is not consistent with the current investigator brochure, or, if an investigator brochure is not required, or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amend. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the investigator brochure only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the investigator brochure only listed cerebral vascular accidents.
312.3	" <i>Disability.</i> A substantial disruption of the person's ability to conduct normal life function.
312.3	<i>Life-threatening adverse drug experience.</i> Any adverse drug experience that places the patient or the subject, in the view of the investigator, at immediate risk of death from the reaction as it occurred, i.e., it does not include a reaction that, had it occurred in a more severe form, might have caused death.
312.3	" <i>Serious adverse drug experience</i> " <p>Any adverse drug experience occurring at any dose that results in any of the following outcomes:</p> <ul style="list-style-type: none"> • Death, • a life-threatening adverse drug experience, • inpatient hospitalization or prolongation of existing hospitalization, • a persistent or significant disability/incapacity, • or a congenital anomaly/birth defect. <p>Important medical events that may not result in death, be life-threatening, or require hospitalization, may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.</p>

