

UPIRTSOs – PERTINENT DEFINITIONS

The following IRB Definitions related to UPIRTSOs come from IRB Policy 18:

Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO): Includes those events that:

- (1) are not expected given the nature of the research procedures and the subject population being studied
- (2) suggest that the research places subjects or others at a greater risk of harm or discomfort related to the research than was previously known or recognized and
- (3) are related or possibly related to the research.

Possibly related: There is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.

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

Serious Adverse Event: Any adverse event that results in any of the following outcomes:

- Death
- A life-threatening adverse event
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant disability/incapacity or a congenital anomaly/birth defect.

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse event 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. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or

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the development of drug dependency or drug abuse.

For VA studies, a Serious Adverse Event (SAE) is an untoward occurrence in human research that results in death, a life-threatening experience, inpatient hospitalization, prolongation of hospitalization, persistent or significant disability or incapacity, congenital anomaly, or birth defect, or that requires medical, surgical, behavioral, social, or other intervention to prevent such an outcome.

Unexpected Adverse Event: As defined by the FDA, any adverse event, 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 amended. 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.

Clarification Note: “Unexpected,” as used in this definition, refers to an adverse event 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 and not listed in the Investigator’s Brochure.

For VA studies,

Unanticipated and unexpected refer to an event or problem in human research that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol documents and the characteristics of the study population.

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For VA studies,

Serious Problem: A serious problem is a problem in human research or research information security that may reasonably be regarded as:

- (1) Presenting a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research personnel, or others, including their rights to privacy and confidentiality of identifiable private information; or
- (2) Substantively compromising a facility's HRPP or research information security program.