

NIH IRB & Research Compliance Review Committee (RCRC) Review of Research Related Events

The NIH IRB and the NIH RCRC each play a role in reviewing research related reportable events.

NIH RCRC:

- Reviews events of possible serious and/or continuing noncompliance (NC) occurring during the conduct of human subjects research (HSR) when NIH is the Reviewing IRB.¹
- Has the final determination whether events constitute serious and/or continuing NC and evaluates corrective action. The RCRC may also suspend or terminate IRB approval of research. They can also suspend new enrollment on studies.
- The NIH RCRC is a duly convened IRB. However, unlike the NIH IRB, the RCRC has a fixed membership and meets monthly as needed.

NIH IRB:

- Reviews events that are possible unanticipated problems (UPs) and any new information that might affect willingness of subjects to enroll or stay on study.
- Reviews any proposed protocol/consent form changes related to the UP or new information.
- Can suspend or terminate approval of HSR in order to protect subject safety. They can also suspend new enrollment on the study.

When the IRB is asked to determine if a reported event is a UP, the Board needs to decide if **ALL 3** criteria are met. The event must:

1. Be **unexpected AND**
2. Be **related or possibly related** to the research **AND**
3. **Places participants or others at a greater risk of harm** than was previously known or expected.

Criterion	IRB considerations based on complete criteria description
Is the event unexpected?	Is the event unexpected in nature, severity, or frequency ² given the following: (a) the research procedures described in the protocol-related documents (e.g., IRB-approved protocol and informed consent document); and (b) the characteristics of the population being studied.
Is the event related or possibly related to the research?	Is the event at least possibly related to the research? (Is there is a reasonable possibility that the event may have been caused by the procedures involved in the research?)
Does the event place participants or others at a greater risk of harm than was previously known or expected?	While the event may have caused harm, it is enough to have caused a greater risk of harm to meet this criterion. <i>Harm</i> is not limited to physical harm. It can also mean psychological, economic or social harm. <i>Others</i> may include research staff, family members or other individuals not participating in the research.

Additional IRB responsibilities: When the IRB determines an event is a UP, IRB members should consider:

- Are corrective actions that are planned or already taken by the investigator appropriate and sufficient?
- Are risks to participants or others still minimized and reasonable in relation to anticipated benefits?
- Are changes to the protocol and/or consent needed? (e.g., Should safety monitoring frequency be increased? Does the consent need to be updated to notify subjects of the new risk? Should existing subjects be reconsented?)
- Are risks such that IRB should consider suspending enrollment? Should the IRB suspend/terminate entire study?

¹ See [NIH IRP HRPP Policy Glossary](#) for of noncompliance that is serious or continuing.

² For example:

- Unexpected **nature**: Participant experiences unexplained severe bleeding while receiving the study agent in an early phase trial. Neither the protocol, consent nor the IB list bleeding as a possible risk.
- Unexpected **severity**: Participant experiences liver failure while taking oral study agent. The IB, protocol and consent list risk of only mild reversible elevation in LFTs
- Unexpected **frequency**: IB and protocol list a 10% risk of possible mild rash requiring topical steroids but at CR, PI notes 25% of participants had such a rash while receiving the study agent

Event for NIH IRB review as possible UP

Is the event unexpected in terms of **nature, severity, or frequency** given the following?

(a) the research procedures described in protocol-related documents or
(b) the characteristics of the subject population being studied

NO

Event is not a UP

YES

Is the event at least possibly related to the research procedures/interventions?

NO

Event is not a UP

YES

Does the event place participants or others at a greater risk of harm than was previously known or expected?

NO

Event is not a UP

YES

Event is a UP



IRB considerations:

- Should consent/protocol be updated?
- Is input from monitoring entity (e.g., DSMB) needed?
- Is corrective action sufficient?
- Is increased safety monitoring required?
- Should IRB suspend enrollment?