

UNANTICIPATED PROBLEMS INVOLVING RISKS TO SUBJECTS OR OTHERS (UPIRTSO)

I. PURPOSE / BACKGROUND

This policy establishes the reporting requirements and the types of unanticipated problems that a University of Louisville (U of L) principal investigator or designee must report to the U of L Institutional Review Board (IRB) to ensure prompt reporting of unanticipated problems involving risks to subjects or others. Regulatory requirements for reporting unanticipated problems involving risks to subjects and others may be found in [45 CFR 46.103\(b\)\(5\)\(i\)](#) and [21 CFR 56.108\(b\)\(1\)](#).

II. DEFINITIONS

Adverse event – any untoward occurrence that may present itself during treatment or administration with a pharmaceutical, therapeutic biologic product or device, and which may or may not have a causal relationship with the treatment.

Department or agency head – the head of any Federal Department or Agency and any other officer or employee of any Department or Agency to whom authority has been delegated.

Event – a problem.

Others – individuals who are not research subjects.

Principal Investigator – the individual responsible and accountable for designing, conducting, and monitoring a human research protocol.

Promptly report - reporting within five (5) workdays when any member of the research team becomes aware of an unanticipated problem or simultaneous with reporting to the sponsor or any other agency or organization, whichever occurs sooner.

Related – more likely than not caused by the research procedures

Risk – the occurrence of harm or a probability that harm might occur. The harm may be physical, psychological, financial, social, economic, or legal.

Serious – An event is serious if it resulted in or required intervention to prevent death, a life-threatening event, injury, hospitalization, prolongation of hospitalization, emergency visit, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect.

Unanticipated problem involving risks to subjects or others – any problem that was unanticipated, was related, and affects the safety and welfare of current or future subjects or others involved with the research. Previously unforeseeable based on the information provided to the IRB.

Unanticipated adverse device effect – 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

Subject: Reporting of Unanticipated Problems Involving Risks to Subjects or Others	Policy and Procedure	Approved: 12-16-2004	1
Author: Institutional Review Board	Effective Date: Final 1-1-2005	Revised Date:	

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. (21 CFR 812.3(s))

Unexpected adverse drug experience - 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 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. “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. (21 CFR 312.32)

III. POLICY

A principal investigator or designee must promptly report any of the following events:

- a. Adverse events related to a drug or device (whether occurring on-site or reported to the investigator by a sponsor or other site), which in the opinion of the principal investigator are:
 - 1. unexpected,
 - 2. serious, and
 - 3. related,
- b. Problems that required prompt reporting to the sponsor or funding agency,
- c. Accidental or unintentional change to the IRB approved protocol that involved risks to subject or others, or that has the potential to recur,
- d. Changes to the protocol taken without prior IRB review to an eliminate apparent immediate hazard to a research subject,
- e. Information (publication in the literature, safety monitoring report, interim result, or other finding) that indicates a change to the risks or potential benefits of the research,
- f. DSMB summary reports that indicate a change to the risks or potential benefits of the research,
- g. Breach of confidentiality of research data,
- h. Incorrect labeling of study medication/test article,
- i. Incorrect dosing of study medication/test article,
- j. Study medication/test article accountability discrepancies that trigger a study subject to be withdrawn from a study,
- k. Breach of privacy/confidentiality/data security/loss of study data/destruction of study data due to noncompliance,
- l. Unauthorized use or disclosure of protected health information (PHI),
- m. Subject complaints that indicate an unanticipated risk, or that cannot be resolved by the research staff,
- n. Incarceration of a subject while participating in research,
- o. Suicide attempt related to participation in a research study,

Subject: Reporting of Unanticipated Problems Involving Risks to Subjects or Others	Policy and Procedure	Approved: 12-16-2004	2
Author: Institutional Review Board	Effective Date: 1-1-2005	Revised Date:	

- p. Death of a healthy volunteer while participating in research or within 30 days of participation,
- q. Injury (needle stick, drug ingestion, chemical exposure, etc.) of study personnel related to preparation or administration of study drug,
- r. Unanticipated adverse device effect, or
- s. Any other event which in the opinion of the principal investigator was:
 - 1. unanticipated,
 - 2. related, and
 - 3. affects the safety and welfare of current or future subjects.

IV. ORGANIZATIONAL RESPONSIBILITIES

Any principal investigator who conducts research under the aegis of the University of Louisville IRBs and the IRB must follow this policy.

V. VIOLATIONS OF THIS POLICY

Failure of investigators to report events as required by this policy could result in a range of penalties. These penalties are outlined in the University's [Administrative Sanctions for Violations of University of Louisville Research Policies](#). This policy may be found on the Research Integrity Program Home Page (<http://www.ori.louisville.edu>) under research policies.

VI. PROCEDURE FOR POLICY

The principal investigator will report to the IRB using the **Event Report Form** (Appendix A) found at the forms link on the Human Subjects Protection Program Office ([HSPPO](#)) website. Principal investigators may also report events by email or letter by providing the same information as requested in the **Event Report Form**.

If, in response to an event report, the IRB chair believes that immediate action is needed to ensure research subject safety; the chair may request that the investigator suspend research procedures or take action to suspend research procedures pending discussion of the event at the next convened meeting of the IRB. Suspensions ordered by the chair will follow IRB policies and procedures regarding suspensions.

Each report will have initial review by a primary reviewer from the Serious Adverse Events Subcommittee (SAES) to determine if the report may be an unanticipated problem involving risks to subjects or others. Members of the SAES will be members/alternates of the IRB.

HSPPO staff will provide the following documents to the SAES primary reviewer:

- a. A copy of the event report and all attachments provided by the investigator,
- b. A copy of the protocol,
- c. A copy of the current informed consent, and
- d. Any other material that the IRB staff believes relevant to the event.

Subject: Reporting of Unanticipated Problems Involving Risks to Subjects or Others	Policy and Procedure	Approved: 12-16-2004	3
Author: Institutional Review Board	Effective Date: 1-1-2005	Revised Date:	

HSPPO staff will retain these documents and the primary reviewer’s notes if the SAES recommendation is to report the event.

If the recommendation is to report the event, the HSPPO staff will schedule IRB review at the next convened meeting whose agenda has not been finalized.

The HSPPO staff will bring the SAES primary reviewer’s, documents to the IRB meeting where the primary reviewer will discuss the report. Should the SAES primary reviewer be unavailable, the IRB chair will lead the discussion.

HSPPO staff will provide the following documents to all other IRB members:

- a. A copy of the event report and all attachments provided by the investigator, and
- b. A copy of the current informed consent.

HSPPO staff will bring the protocol file to the meeting.

The SAES primary reviewer will present a summary of the problem and make a recommendation to the IRB about whether the event represents an unanticipated problem involving risks to subjects or others. The IRB will deliberate and vote to determine whether the event represented an unanticipated problem involving risks to subjects or others. The determination of whether an event represents an unanticipated problem is based on whether the event represents all of the following:

- a. Was unanticipated,
- b. Was related, and
- c. Affects the safety and welfare of current or future subjects.

If the SAES primary reviewer determines that the problem (see III. Policy) was unanticipated, was related to the research and affects the safety and welfare of current or future subjects or others involved with the research, the reviewer will make a recommendation to the IRB about proposed actions. The IRB will deliberate and vote to approve these or any other appropriate actions. Actions the SAES primary review and IRB should consider include, but are not limited to:

- a. Requiring no action,
- b. Requiring changes in informed consent documents,
- c. Requiring changes in the protocol or other study documents,
- d. Requiring re-consenting or informing current or previously enrolled research subjects (to occur whenever the information may relate to subjects willingness to continue participation in the research,
- e. Requiring steps to reduce any immediate risks to subjects or others,
- f. Modifying the continuing review schedule,
- g. Suspending or terminating the research study (according to the IRB policy and procedure regarding suspensions and terminations),
- h. Requesting more information pending a final decision,
- i. Referring to other organizational entities (e.g., legal counsel, risk management, institutional official), or

Subject: Reporting of Unanticipated Problems Involving Risks to Subjects or Others	Policy and Procedure	Approved: 12-16-2004	4
Author: Institutional Review Board	Effective Date: 1-1-2005	Revised Date:	

- j. Taking other actions appropriate for the local context.

VII. REPORT OF FINDINGS

Follow the University of Louisville IRB Report of Findings policy for reporting unanticipated problems involving risks to subjects or others. This policy is located on the [HSPPO](#) website under Research Related Policies.

Subject: Reporting of Unanticipated Problems Involving Risks to Subjects or Others	Policy and Procedure	Approved: 12-16-2004	5
Author: Institutional Review Board	Effective Date: 1-1-2005	Revised Date:	

EVENT REPORT FORM

Use this form to report events that require reporting according to the IRB policy and procedure Unanticipated Problems Involving Risks to Subjects or Others (UPIRTSO). Call the IRB Office for assistance (502-852-5188).

U of L IRB Protocol Number: _____ **Sponsor Protocol Number:** _____

INVESTIGATOR: _____

COORDINATOR (if assisting in completing the form): _____

ADDRESS: _____

PHONE Number of Contact Person: (____) _____

STUDY TITLE: _____

Date(s) that problem occurred: _____ **Date Reported to the Sponsor:** _____

Study site where problem occurred (if known): _____

The Principal Investigator or designee should answer the following questions.

Provide a brief description of the problem.

If able, tell why the problem occurred? What were the circumstances?

Describe steps taken to resolve the problem and procedures implemented to avoid similar problems in the future.

In the investigator's opinion was this event unanticipated? _____ **Yes** _____ **No**

In the investigator's opinion was this event related to the research? _____ **Yes** _____ **No**

Does this problem affect the safety or welfare of current or future subjects? _____ **Yes** _____ **No**

If yes, please describe:

Has this problem been reported to someone or some organization other than the sponsor and the appropriate University of Louisville IRB? _____ **Yes** _____ **No**

If yes, to whom has the problem been reported?

_____/_____/_____
SIGNATURE Person Reporting Problem **DATE**

Subject: Reporting of Unanticipated Problems Involving Risks to Subjects or Others	Policy and Procedure	Approved: 12-16-2004	6
Author: Institutional Review Board	Effective Date: 1-1-2005	Revised Date:	