Status **Active** PolicyStat ID **16196420**

Origination	01/2023
Last Approved	10/2024
Effective	10/2024
Next Review	10/2026
Owner	Trudy Wittenberg: 4388 Institutional Review Board Administrator
Department	HRPP/Research

Research: Unanticipated Problems & Serious Adverse Events Reporting- AD.0193

PURPOSE

The purpose of this policy is to describe the procedures for processing reports of unanticipated problems involving risks to participants or others and **adverse events** submitted to the IRB. Our policies guide our practices and ensure that we place people at the heart of all we do to deliver the best outcomes and safest care.

APPLICABILITY

This policy applies to Lakeland Regional Health's **Workforce** and research personnel engaged in research.

POLICY

I. **General**

A. Federal regulations require the IRB to ensure that investigators promptly report "any **unanticipated problems involving risk to subjects or others**." 45 CFR § 46.108(4)(i); and 21 CFR § 56.108(b)(1).

B. Unanticipated problems or adverse events can occur in any type of research (medical or social/behavioral/educational research). Some events are expected (e.g., lightheadedness during blood collection), while others are unexpected (theft of devices containing data). Events also vary in seriousness and the extent to which they are **related to the research**. Reporting **serious adverse events** and unanticipated problems facilitates protection of research participants by allowing investigators and the IRB to determine whether the event/problem indicates changes are necessary to minimize risk, ensure the risk/benefit ratio remains favorable, and ensure participants are fully informed.

II. **Investigator Reporting Requirements and Timelines**

A. Investigators must promptly report to the IRB:

1. Any serious adverse event that is related or possibly related to the research; or
2. Any event that meets the definition of an **unanticipated problem**.

B. In general, "prompt" reporting means within ten (10) days of an occurrence or within one (1) week of the principal investigator (PI) becoming aware of an occurrence.

C. If applicable, reporting must also follow the requirements and timelines set forth in data safety and monitoring plans that are in place for the research.

D. Follow-up reports on previous events should be reported if the initial event itself met the IRB's definition of a serious adverse event or if the follow-up report adds value to the initial report.

E. For non-local serious adverse events and unanticipated problems, a log will be compiled and submitted at continuing review.

III. **Immediate Risk of Serious Harm**

A. If the problem poses an immediate risk of serious harm to a participant or others, it must be reported immediately to the IRB Office via phone at 863-687-1100 x7214.

IV. **Federally Funded or Supported Research**

A. Some federal agencies require investigators to report adverse events or unanticipated problems to the agency within specified timeframes — immediately in certain instances. Investigators should ensure they are familiar with these requirements.

V. **Medical Devices and New Drugs**

A. For research on medical devices, an **unanticipated adverse device effect** (UADE) must be reported to the IRB and the sponsor as follows:

1. A report of a UADE must be submitted to the sponsor and the reviewing IRB as soon as possible but not later than ten (10) working days after the investigator first learns of the effect (21 CFR § 812.150(a)(1)).
2. Sponsors must immediately conduct an evaluation of a UADE and must report the results of the evaluation to the FDA, all reviewing IRBs, and participating investigators within ten (10) working days after the sponsor first receives notice of the effect (21 CFR § 812.46(b), 21 CFR § 812.150 (b)(1)).

B. Investigators conducting clinical investigations of drug or biological products under an investigational new drug (IND) application or investigational medical devices under an FDA Investigational Device Exemption (IDE) must also report certain types of adverse events and unanticipated problems to the sponsor and/or FDA. Investigators are encouraged to carefully review the IRB's policy on Investigational Drugs and Investigational Devices and to consult with their sponsors to learn more about these requirements.

VI. **Relationship Between Adverse Events and Unanticipated Problems**

A. An unanticipated problem is by definition unexpected, whereas an adverse event may be either expected or unexpected. Unanticipated problems may or may not be adverse events. Adverse events relate to harm to participants; unanticipated problems may involve an increased risk of harm even if no actual harm occurred.

B. Examples of reportable unanticipated problems (which may or may not be adverse events) include, but are not limited to:

1. A breach in confidentiality resulting from disclosure of confidential information or from lost or stolen confidential information that may involve risk to the subjects or others;
2. Complaint of a participant or family member that indicates an unanticipated risk;
3. Harm or risk of harm to research staff;
4. Laboratory or medication errors that may involve potential risk to the individual or others;
5. Disqualification or suspension of investigators;
6. Accidental or unintentional change to the IRB-approved protocol that involves risks or has the potential to recur;
7. Deviation from the IRB-approved protocol without prior IRB review to eliminate apparent immediate hazard to a research participant;
8. Any deviation from the IRB-approved protocol that increases risk or affects the participants' rights, safety, or welfare; or
9. Newly discovered information (publication in literature, a safety monitoring report, a revised investigator's brochure, interim results, or other finding) that indicates a change in the risk/benefit ratio of the research.

C. Any adverse event must be reported (whether or not it is serious) if it meets the definition of an unanticipated problem (i.e., unexpected, related to the research, suggests increased risk of harm to subjects or others). In general, the following types of adverse events are considered to be unanticipated problems that must be reported to the IRB:

1. Single occurrence of a serious, unexpected event that is strongly associated with the research;
2. Multiple occurrences of an adverse event that, based on aggregate analysis, is determined to be an unanticipated problem. There should be a determination that the series of adverse events represents a signal that the adverse events were not just isolated occurrences and involve risk to human subjects (e.g., a comparison of rates across treatment groups in the drug treatment arm versus a control); or
3. An expected adverse event (that is described in the investigator's brochure, protocol, or informed consent documents) that occurs at a severity or rate/frequency that is inconsistent with prior observations.

PROCEDURE

I. **IRB Process for Handling Reported Problems**

A. Upon review of the report, the IRB Administrator or IRB Chair will (a) determine if the report includes the necessary information, (b) perform an initial evaluation, and (c) consult with appropriate individuals (e.g., physician consultant, IRB Chair, etc.) if necessary.

B. If, in the judgment of the IRB Administrator or IRB Chair, participants or others may be at immediate risk of harm and there is insufficient time to wait for review by the convened IRB, the IRB Administrator or the IRB Chair will require the principal investigator to suspend the study pending review by the convened IRB.

C. If participants or others are not at immediate risk, the report is scheduled for review at the next meeting of the convened IRB.

D. The convened IRB determines whether the incident constitutes an unanticipated problem involving risks to subjects or others, and specifies any corrective actions. Corrective actions may include, but are not limited to the following:

1. Acknowledgement/acceptance without further recommendation;
2. A request for further clarification or a corrective action plan from the investigator;
3. Changes in the protocol (e.g., additional tests or visits to detect similar events in a timely fashion; changes to the confidentiality measures employed in the study, changes to inclusion/exclusion criteria);
4. Changes to the informed consent document(s);
5. Notification to enrolled subjects and/or re-consenting when appropriate;
6. A change in frequency of continuing review;
7. Further inquiry into other protocols utilizing particular dietary supplements, devices, or procedures in question;
8. Additional training for investigators and/or research staff;
9. Monitoring of the research procedures or informed consent process;
10. Referral to other organizational entities (e.g., Research Council);
11. Suspension or termination of IRB approval for the study; and
12. Post-approval monitoring or other monitoring actions deemed appropriate by the IRB.

E. If the IRB acknowledges/accepts the report and deems that no further follow-up is required, the IRB Administrator will notify the PI of the review outcome.

F. If the committee requests clarification(s), additional information or revisions to the approved protocol, the IRB Administrator will notify the PI of the need for additional information and/or changes.

G. Adverse events or unanticipated problems that also involve deviations from the IRB-

approved protocol are reviewed in accordance with the IRB Review of Protocol Deviations and Noncompliance.

H. If the IRB determines the problem/event to be an unanticipated problem involving risks to subjects or others, the IRB Administrator reports the IRB's determination to federal agencies or sponsors in accordance with federal regulations. The IRB Administrator also reports the IRB's determination to the appropriate Institutional Official, and Legal Affairs & Risk, along with the filing of an RL report.

I. If the event is a serious adverse event and/or meets the definition of a Sentinel Event as defined by the policy **Sentinel Events: Identification, Investigation, and Reporting- AD.00114**, then the event should be reported to Risk Management for further discussion/follow up as needed. The report to Risk shall be completed by the IRB Chair or IRB Administrator.

ABBREVIATIONS

AE: Adverse Event

FDA: Food & Drug Association

HIPAA: Health Insurance Portability and Accountability Act

IRB: Institutional Review Board

LAR: Legally Authorized Representative

PHI: Private Health Information

SAE: Serious Adverse Event

UAP: Unanticipated Problem

DEFINITIONS

I. **Adverse event**: Any unfavorable occurrence in a research participant that is temporally associated with the participant's involvement in the research. An adverse event encompasses physical, psychological, social, economic, legal, or informational harms. It may or may not be directly related to the individual's participation in the research.

II. **Anticipated problem/adverse event**: Any foreseen or expected problem/event that was described in the IRB-approved research protocol, any applicable investigator brochure, and/or the current IRB-approved informed consent document.

III. **Minimal Risk**: Probability and magnitude of harm or discomfort anticipated are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

IV. **Related or possibly related to the research**: An event is considered related to the research if, in the opinion of the investigator, it was more likely than not the result of the research interventions/interactions, or the result of the collection/use of identifiable private information for the research (i.e., there is a reasonable possibility that the event may have been caused by participation in the research).

V. **Serious adverse event**: Any adverse event temporally associated with the individual's participation in research that meets any of the following criteria:

   A. Results in death;

   B. Is life threatening (places the subject at immediate risk of death from the event as it occurs);

   C. Requires inpatient hospitalization or prolongation of existing hospitalization;

   D. Results in a persistent or significant disability/incapacity;

   E. Results in a congenital anomaly/birth defect;

   F. Based upon appropriate medical judgment, may jeopardize the individual's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition;

   G. Results in a breach of confidentiality that is damaging to the participant's rights, employment, financial standing or reputation; or

   H. Causes significant psychological, social, economic, or legal harm to the participant or others.

VI. **Unanticipated adverse device effect (UADE)**: For studies of medical devices, the investigational device exemption regulations define an unanticipated adverse device effect as any serious effect on health or safety or any lifethreatening 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 (21 CFR § 812.3(s)).

VII. **Unanticipated problems involving risks to subjects or others**: Any incident, experience, or outcome that meets all of the following criteria:

   A. Is unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;

   B. Is related or possibly related to an individual's participation in the research; and

   C. Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, social, economic, legal, or informational harm) than was previously known.

VIII. **Unexpected adverse event**: Any adverse event occurring in one or more participants when the nature, severity, or frequency is not consistent with either:

   A. The known or foreseeable risk described in (a) the protocol-related documents (i.e., the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document); and (b) other relevant sources of information (e.g., product labeling and package inserts); or

   B. The expected natural progression of any underlying disease, disorder, or condition of the individuals(s) experiencing the adverse event and the individual's predisposing risk factor profile for the adverse event.

IX. **Workforce**: All LRH employees, volunteers, trainees/students, contractors, and Medical Staff.

REFERENCES

I. 45 CFR § 46.108
II. 21 CFR § 56.108
III. 21 CFR Part 812
IV. reporting-adverse-unanticipated.pdf (iastate.edu)

Approval Signatures

Step Description	Approver	Date
	Danielle Drummond: 0001 President & Chief Executive Officer - LRHS	10/2024
	Jonn Hoppe: 1011 Executive VP, Chief Legal Officer-General Cou	10/2024
	Timothy Regan: 0009 President - LRMC/Chief Medical Officer	10/2024
	Renee Reed: 4064 Senior Attorney	10/2024
	Deana Nelson: 4080 SVP - Administration and Corporate Initiative	09/2024
	Stacy Carrozza: 4621 AVP - Associate General Counsel	08/2024
	Georgia Ann Keriazes: 0729 QI/ Due Pharmacist	08/2024
	Andrew Bugajski: 4387 AVP - Research and Sponsored Studies	08/2024