

Investigators must promptly report to the IRB all unanticipated problems involving risks to research subjects or others and serious adverse events possibly related to research participation. The IRB reviews reports to consider whether the risk:benefit ratio remains favorable, as well as the need for any further corrective actions to protect the safety, rights and welfare of future, current, and/or prior research participants.

1.0 Problems and events requiring prompt reporting.

Investigators or research team members are required to report to the IRB within 72 hours of knowledge of the following unanticipated problems or serious adverse events, whether occurring during ongoing research, after research completion, or after participant withdrawal:

1.1 Unanticipated problems.

Possible unanticipated problems that involve risks to subjects or others (hereafter referred to as 'unanticipated problems') require prompt reporting to the IRB. Such unanticipated problems need not have resulted in actual harm to subjects, but may only represent increased risk of harm (e.g., physical, psychological, social, economic, legal). Examples may include:

- breach of confidentiality or privacy (e.g., lost or stolen research data)
- attempted suicide of a research participant possibly related to research participation
- threat to participants or others related to their research participation
- change in the environment that increases risk (e.g., political or social changes)
- identification of previously unforeseen risk to participants, as reported in the literature, and/or identified through a safety monitoring report or interim result
- change implemented (without prior IRB approval) to prevent immediate harm
- accidental or unintentional deviation from protocol that involved risks or has the potential to recur
- complaint from participant(s) or others

1.2 Adverse events.

Those adverse events that constitute unanticipated problems, or are of a serious nature require prompt reporting to the IRB. These events may include, but are not limited to:

- serious injury or reaction requiring medical intervention
- life-threatening condition or death
- hospitalization
- persistent or significant disability
- congenital anomaly

2.0 Other problems and events

Those problems and non-serious adverse events that were anticipated to occur with a certain severity and frequency do not require a prompt report (unless otherwise required by a sponsor). The risk of these problems and events would have already been described in the protocol form, and disclosed to participants in the consent process, and their occurrence may be summarized

in a continuing review or monitoring report. Some examples of problems that may be expected to occur in some research include, but are not limited to:

- mild allergic reactions to a topical gel
- transient minor headaches
- temporary muscle soreness after prolonged or intense exercise
- slight bruising after a blood draw
- transient feelings of anxiety

3.0 Submission of report.

The investigator or research team member notifies the IRB within 72 hours of knowledge of the problem, providing the following information on the *Report of Unanticipated Problem or Serious Adverse Event* form:

- type of problem
- all relevant details of the problem or adverse event
- a description of any immediate or proposed actions taken to protect the rights, safety and welfare of subjects

Other parties (research participants or others) who have knowledge of possible unanticipated problems or serious adverse events associated with an NDSU research project may also submit an oral or written report to the IRB office.

4.0 IRB Review.

Upon receipt, HRPP staff promptly forward the report to the IRB Chair or designee for initial review, and to determine the need for any immediate action. The originally approved protocol, consent document(s) and/or any other relevant materials may be reviewed using the criteria as described below in section 4.2. The IRB Chair or designee may communicate with the PI to obtain additional information, and/or require a directed audit of the research, in accordance with SOP 12.2, *Directed Audits of Research*. All communication and determinations are documented in writing.

4.1 Assignment for review.

The IRB Chair or designee determines the appropriate level of review for the report.

4.1.1 Expedited review:

If the problem involves no more than minimal risks to participants, the IRB Chair or designee may determine that expedited review is appropriate, in accordance with SOP 7.3 *Expedited Review*. IRB members are notified of the review and outcome as an agenda item for the next convened meeting.

4.1.2 Review by IRB subcommittee.

The IRB Chair or designee may direct that a subcommittee review the report prior to consideration by the full board. All communications are documented in writing, and the subcommittee provides a written report to the board, including recommended corrective actions as applicable.

4.1.3 Review at convened meeting of IRB.

At a convened meeting, the IRB reviews reports referred from the IRB Chair, designee or IRB subcommittee. The IRB Chair or designee and another member are assigned as primary reviewers; a determination is made by applying the criteria described in 4.2. The IRB may invite the investigator and members of the research team to attend the meeting or provide additional information about the problem.

4.2 Criteria for review.

Regardless of level of review, the following criteria are applied during review of the report of unanticipated problems or adverse events.

4.2.1 Criteria for approval.

The IRB considers whether the requirements for approval of the research continue to be met, particularly whether risks to subjects are still minimized and reasonable in relation to the anticipated benefits.

4.2.2 Corrective actions.

In addition to any corrective actions implemented or proposed by the investigator, the IRB may determine that additional corrective actions are necessary to meet criteria for continuing IRB approval, prevent recurrence of the problem, and protect the rights, safety and welfare of prior, current and/or future participants. These corrective actions may include, but are not limited to:

- revision of inclusion or exclusion criteria
- revision to data safeguarding procedures
- implementation of new, or additional monitoring procedures
- changes to the consent document(s) to include newly recognized risks
- notification or re-consent of previous participants
- notification to current participants (required when the information may relate to participants' willingness to continue to take part in the research)
- modification of the continuing review period (i.e. more frequently than once/year)

When necessary to eliminate apparent immediate hazards to participants, the investigator or research team may implement corrective actions without prior review by the IRB.

4.3 Termination or suspension of research.

At any point during IRB review, a determination may be made that suspension or termination of the research is necessary to protect the safety, rights and welfare of research participants. The investigator or research team member may also take this action voluntarily. Suspension or termination may be warranted if the report suggests subjects have experienced unexpected serious harm, or their rights and welfare have been severely negatively impacted. The following parties are promptly notified in writing:

- investigator and research team
- NDSU Department Chair/Head
- Institutional Official (IO)
- Sponsored Programs Administration, if funded

The IO subsequently reports to OHRP and external entities, as applicable, in accordance with SOP 12.4 *Reporting Noncompliance, Suspensions, Terminations and Unanticipated Problems*.

5.0 Notification of IRB action.

The IRB Chair or designee, with the assistance of HRPP staff, promptly send written notice, including the reason for the IRB's action, to:

- investigator and research team
- NDSU Department Chair/Head

6.0 Determination regarding additional reporting.

An unanticipated problem or serious adverse event is subject to additional prompt reporting when:

- unexpected (in terms of nature, severity, or frequency);
- related or possibly related to participation in the research; and
- determined to involve greater risks to subjects than previously known.

If all criteria are met, the issue is subject to federal regulations requiring additional prompt reporting, as described in SOP 12.4 *Reporting Noncompliance, Suspensions, Terminations and Unanticipated Problems*.

DEFINITIONS:

Unanticipated problem: any incident, experience, or outcome that meets all the following criteria:

- is unexpected (in terms of nature, severity, or frequency) given the characteristics of the subject population and the research as described in the IRB approved protocol and consent document(s)
- is related, or possibly related to participation in the research
- suggests the research places subjects or others at greater risk of harm (physical, psychological, economic, or social harm) than previously known or recognized

Adverse event: any untoward or unfavorable medical occurrence (physical or psychological) in a human subject, including any abnormal sign, symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to their research participation

Serious adverse event: any adverse event that meets any of the following criteria:

- results in death
- is life-threatening
- requires hospitalization
- results in persistent or significant disability
- results in congenital anomaly
- may jeopardize subject's health and may require medical intervention to prevent any of the other outcomes listed here

Risk: the probability of harm or discomfort; may include physical, psychological, social, economic, legal, or other harms

REFERENCES:

[45CFR46.111\(a\)](#) Criteria for IRB approval of research

[21CFR56.111\(a\)](#) Criteria for IRB approval of research

[45CFR46.103\(b\)\(5\)](#) Written procedures

[21CFR56.108\(b\)](#) IRB Functions and Operations

[45CFR46.113](#) Suspension or termination of IRB approval of research

[OHRP FWA Assurance Training](#)

[Terms of the FederalWide Assurance](#)

[FDA Guidance: Adverse Event Reporting to IRBs – Improving Human Subject Protection](#)

RELATED FORMS:

Report of Unanticipated Problem or Serious Adverse Event

RELATED HRPP SECTIONS:

7.2 Criteria for IRB Approval

7.3 Expedited Review

12.2 Directed Audits of Research

12.4 Reporting Noncompliance, Suspensions, Terminations and Unanticipated Problems