

7 IRB Review of Research:

7.7 Unanticipated Problems and Serious Adverse Events

Effective Date: **6/12/2009**

Revised:

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, 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 problems or 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 (ie., physical, psychological, social, economic, legal).

1.2 Adverse events

Those adverse events that constitute unanticipated problems, or are of a serious nature require prompt reporting to the IRB.

1.3 Examples:

Some examples of the types of problems and events that require prompt reporting may include, but are not limited to:

- inadvertent breach of confidentiality or privacy (ie, lost or stolen research data)
- serious or unexpected injury or reaction
- attempted suicide of a research subject possibly related to research participation
- unexpected participant harm that is possibly related to the research
- threat to participants or others related to their research participation
- change in the research environment that increases risk (ie, 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 change that involved risks or has the potential to recur
- complaint from participants or others

2.0 Other problems and events:

Other problems and non-serious adverse events that were previously expected to occur in a research project do not require prompt reporting (unless otherwise required by a sponsor). The expected nature, severity and frequency of such risks would have already been described in the protocol form, and disclosed to participants in the consent process. The IRB may also have required a monitoring plan for research involving more than minimal risk to participants. While prompt reporting is not required, these problems and events should be summarized in the

continuing review report to the IRB. 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

The problems that are expected to occur with a certain frequency and severity that are described in the protocol form, and disclosed to participants in the consent document would not require prompt reporting. However, a breach of confidential, sensitive data is always considered serious and requires prompt reporting.

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 of Reports:

4.1 Review by IRB Chair or designee:

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 chair may review the originally approved protocol, consent document(s) or any other relevant materials, communicate with the PI for additional information, and/or require a directed audit of the research. All communication and determinations will be documented in writing. Possible actions include:

4.1.1 Termination or suspension of research:

The IRB Chair or designee may immediately suspend approval of the research if the report suggests subjects have experienced unexpected serious harm, or their rights and welfare have been negatively impacted. The IRB Chair or designee, with the assistance of HRPP staff will promptly send written notice, including the reason for the IRB's action, to the:

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

The IO will subsequently report to OHRP and external entities, as applicable, in accordance with *12.4 Reporting*.

4.1.2 Expedited review:

If the problem involves no more than minimal risks to participants, the IRB Chair or designee may review, or assign an experienced member to review, the report by the expedited method, in accordance with *7.3 Expedited Review*. The reviewer will receive a copy of the report, the approved protocol, and any other relevant information, and may request additional information from the investigator as needed. The review will encompass the considerations, possible actions and reporting as described in 4.4 and following sections below. IRB members will be notified of the review and outcome as an agenda item for the next convened meeting.

4.2 Review by IRB subcommittee:

The IRB Chair or designee may direct that a subcommittee review the problem prior to consideration by the full board. A subcommittee comprised of at least 3 members, including the IRB Chair or designee, selected members, and HRPP staff may obtain additional information from the investigator, require a directed audit of research, or obtain any other additional information as appropriate. All communications are documented in writing, and the subcommittee provides a written report to the board, including recommended corrective actions as applicable. The subcommittee may also immediately suspend or terminate the research if subjects have experienced serious harm, or the research negatively impacts the rights or welfare of subjects. The suspension or termination is promptly reported as described in *12.4 Reporting Noncompliance, Suspensions, Terminations and Unanticipated Problems*.

4.3 Review at convened meeting of IRB:

At a convened meeting, the IRB considers reports of unanticipated problems referred from the IRB Chair, designee or IRB subcommittee.

4.3.1 Materials for review:

The board reviews the report, approved protocol and consent document(s), and any additional information, including subcommittee report and recommendations, as applicable. The IRB Chair or designee and another member are assigned as primary reviewers; the information is provided to board members as soon as possible prior to a convened meeting.

4.3.2 Consultation with investigator and research team:

The IRB may invite the investigator and members of the research team to attend the meeting or provide additional information about the problem.

4.3.3 Determination regarding suspension or termination of the research:

The IRB may determine that research must be suspended or terminated in order to protect the rights, safety and welfare of research participants. If the IRB Chair, designee or subcommittee has already suspended approval for the project, the IRB determines whether to lift, or continue the suspension, or terminate the project to protect subject safety.

4.4 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. The IRB may determine that corrective actions are necessary to meet the criteria for IRB approval, and prevent recurrence of the problem. 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
- other changes to the protocol or consent
- other corrective actions as necessary
- no action necessary

4.5 Other corrective actions:

The IRB considers whether the problem would require other corrective actions to protect the rights, safety and welfare of prior, current, or future participants. The IRB may require additional corrective actions, which may include, but are not limited to:

- 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 (more frequently than once/yr)
- monitoring of the research or consent process
- other corrective actions as necessary
- no further actions

4.6 Notification of IRB action:

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

- investigator and research team
- NDSU Department Chair/Head

4.7 Determination regarding additional reporting:

The IRB considers whether or not the problem meets all the following criteria:

- is unexpected (in terms of nature, severity, or frequency)
- is related or possibly related to participation in the research
- suggests that the research poses greater risks to subjects than previously known

If all criteria are met, the issue is subject to federal regulations requiring additional prompt reporting to the Institutional Official (IO), as well as OHRP, other federal agencies, including federal funding sponsors, as applicable. The IRB Chair or designee, with the assistance of HRPP staff, will promptly send a written notice to the IO.

5.0 Notification of Institutional Official (IO) and further reporting:

Upon written notice from the IRB Chair or designee of unanticipated problems involving risks to subjects or others, or serious adverse events, the IO may:

- accept the report and promptly report further to external entities
- require additional corrective actions and promptly report further to external entities
- require additional investigation
- suspend or terminate the research, unless already suspended or terminated

The IO, with the assistance of HRPP staff, submits required reports to OHRP, federal funding sponsors, and other federal agencies (ie, FDA) as applicable. Refer to *12.4 Reporting Noncompliance, Suspensions, Terminations and Unanticipated Problems*.

DEFINITIONS:

Unanticipated problem: an unanticipated problem that involves risks to subjects or others is 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) that 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 risks

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 Guidance on Written Procedures, January 2007](#)

[OHRP FWA Assurance Training](#)

[Terms of the FederalWide Assurance](#) #4, Written Procedures

[OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events](#)
[FDA Guidance: Adverse Event Reporting to IRBs – Improving Human Subject Protection](#)

RELATED [FORMS](#):

Report of Unanticipated Problem or Serious Adverse Event

RELATED HRPP SECTIONS:

12.4 Reporting Noncompliance, Suspensions, Terminations and Unanticipated Problems