

SOP: 407
UNANTICIPATED PROBLEMS INVOLVING
RISKS TO PARTICIPANTS OR OTHERS
AND PROTOCOL DEVIATIONS

1. POLICY

The Institutional Review Board (IRB) requires investigators to promptly report any unanticipated problem that involves risks to participants or others. Unanticipated problems involving risks to participants or others include any problems that (1) were unforeseen at the time of occurrence and (2) indicate that participants are at increased risk of harm.

The IRB requires investigators to report protocol deviations. Protocol deviations are events that are a departure from the specific protocol procedures approved by the IRB. Protocol deviations may or may not place participants at risk.

Specific Policies

1.1 Unanticipated Problems Involving Risks to Participants or Others

Investigators are required to submit to the IRB within five business days any unanticipated problems involving risks to participants or others.

There is a high probability that the following problems/events represent unanticipated problems involving risks to participants or others. However, this list is not exhaustive.

- Any harm experienced by a participant, which in the opinion of the investigator is both unexpected and related, regardless of whether the harm was an on-site or off-site adverse event, and regardless of whether the harm was a serious or non-serious adverse event.
- Information that indicates a change to the risks or potential benefits of the research. For example:
 - An interim analysis or safety monitoring report indicates that frequency or magnitude of harms or benefits may be different from that initially presented to the IRB.
 - A paper is published from another study that shows that the risks or potential benefits of the research may be different from that initially presented to the IRB.
- A breach of confidentiality of the study data than was previously known or recognized.
- A change to the protocol made without prior IRB review to eliminate an apparent immediate hazard to a research participant.
- Incarceration of a participant in a protocol not approved to enroll prisoners.
- A sponsor-imposed study suspension due to risk to participants.
- A complaint by a participant when the complaint indicates unexpected risks or cannot be resolved by the research team.

- A protocol violation (meaning an accidental or unintentional change to the IRB approved protocol) that harmed participants or others or that indicates participants or others may be at increased risk of harm.
- A change in FDA labeling or FDA withdrawal from marketing of a drug, device, or biologic used in the research protocol.
- An unanticipated adverse device effect (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 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 and welfare of participants).

It is within the authority of the IRB to institute IRB site visits to promote research integrity if the IRB receives an excessive number of unanticipated problems involving risks to participants or others or protocol deviations or if the IRB independently suspects noncompliance or improprieties on the part of the investigator and/or research team.

1.2 Determination of an Unanticipated Problem Involving Risks to Participants or Others

If the IRB Chair or designee determines and documents on the Unanticipated Problem Report form that the problem/event is an unanticipated problem involving risks to participants or others or the problem/event resulted from serious or continuing noncompliance, the IRB Administrator shall place the event on the agenda of the next available IRB meeting for review.

If the IRB Chair or designee determines and documents on the Unanticipated Problem Report form the problem/event is not an unanticipated problem involving risks to participants or others, the IRB Chair or designee shall complete the review by the expedited procedure.

1.3 Review of an Unanticipated Problem Involving Risks to Participants or Others by the Convened IRB

In reviewing unanticipated problems, the convened IRB shall use the primary and secondary reviewer system, as described in SOP 403, Initial Review - Criteria for IRB Approval. The Unanticipated Problem Report form will be distributed to all Board members as per SOP 302, Administrative Review and Distribution of Materials. The IRB file will be available at the Board meeting for review. The possible actions that could be taken by the IRB include, but are not limited to:

- Modifying the protocol.
- Modifying the information disclosed during the consent process.
- Providing additional information to past participants.
- Notifying current participants when such information might relate to participants' willingness to continue to take part in the research.
- Requiring that the current participants re-consent to participation.
- Modifying the continuing review schedule.

- Monitoring the research.
- Monitoring the consent.
- Suspending the research.
- Terminating the research.
- Referring to other organizational entities (e.g., VA Research and Development Committee, Radiation Safety Committee).
- Obtaining additional information.

The IRB shall review by the convened IRB, more than minor modifications to previously approved research in response to unanticipated problems involving risks to participants or others.

If the IRB determines that the problem is an unanticipated problem involving risks to participants or others, the IRB shall report such problems in accordance with the SOP 308, Reporting to Regulatory Agencies and Institutional Officials.

1.4 Review of Protocol Deviations

When a deviation occurs, the investigator shall complete and submit the Protocol Deviation Report form to the IRB. If, in the investigator's opinion, the deviation meets the criteria for an unanticipated problem involving risks to participants or others, the investigator shall complete Section VI of the Protocol Deviation Report form. The IRB Chair or designee shall also make the determination if the protocol deviation meets the definition of an unanticipated problem involving risks to participants or others.

If the IRB Chair or designee determines and documents on the Protocol Deviation Report form that the deviation is an unanticipated problem involving risks to participants or others or the deviation resulted from serious or continuing noncompliance, the IRB Administrator shall place the deviation on the agenda of the next available IRB meeting for review.

If the IRB Chair or designee determines and documents on the Protocol Deviation Report form that the deviation is not an unanticipated problem involving risks to participants or others, the IRB Chair or designee shall complete the review by the expedited procedure.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

It is the responsibility of the HRPD Director and IRB Chair to review all unanticipated problems involving risks to participants or others to determine if the event should be reported in accordance with SOP 308, Reporting to Regulatory Agencies and Institutional Officials.

IRB Chair or designee is responsible for providing IRB members adequate submission review training and ongoing guidance and for selecting one Primary and one Secondary reviewer with the relevant expertise to perform reviews and make necessary recommendations on approval decisions by the IRB. If the IRB Chair or designee cannot select Primary and Secondary reviewers with the relevant expertise,

the IRB Chair or designee shall defer the review to another IRB with Primary and Secondary reviewers with the relevant expertise or obtains consultation to obtain that expertise.

Investigators involved in human participant research shall report all unanticipated problems involving risks to participants or others to the IRB. Investigators involved in human participant research shall report all protocol deviations.

The IRB Chairs are responsible to review reports of unanticipated problems involving risks to participants and others and protocol deviations and forward them to the convened IRB when appropriate.

4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.103,109
21 CFR 56.108,109

5. REFERENCES TO OTHER APPLICABLE SOPS

SOP 301, Research Submission Requirements
SOP 302, Administrative Review and Distribution of Materials
SOP 308, Reporting to Regulatory Agencies and Institutional Officials
SOP 403, Initial Review – Criteria for IRB Approval
SOP 901, Quality Improvement Program.

6. ATTACHMENTS

407-A Unanticipated Problem Report Form-HSC
407-A-1 Unanticipated Problem Report Form-NC
407-B Protocol Deviation Report Form-HSC
407-B-1 Protocol Deviation Report Form-NC
407-C Instructions for Unanticipated Problems

7. PROCESS OVERVIEW

The IRB Staff confirms that all documents are reviewed for submission per SOP 301, Research Submission Requirements.

The IRB Administrator provides to the IRB Chair, designee, or the convened IRB the items to be reviewed and the tools to conduct the review.

7.1 Review Procedures for Unanticipated Problems Involving Risks to Participants or Others:

HSC campus: If the IRB Chair or designee determines and documents on the Unanticipated Problems Report form that the event is not an unanticipated problem involving risks to participants or others and the event is not a result of serious or continuing noncompliance, the IRB Chair or designee shall indicate withdrawal of the event.

HSC campus: The IRB Administrator updates the database, prints the withdrawal letter, and presents the letter to the IRB Chair for signature (see Attachment 407-C, Instructions for Unanticipated Problems).

Norman campus: If the IRB Chair or designee determines and documents on the Unanticipated Problems Report form that the event is not an unanticipated problem involving risks to participants or others and the event is not a result of serious or continuing noncompliance, the IRB Chair or designee shall indicate the event is approved under expedited review procedures.

If the IRB Chair or designee determines and documents on the Unanticipated Problem Report Form that the problem/event is an unanticipated problem involving risks to participants or others or the problem/event resulted from serious or continuing noncompliance, the IRB Administrator places the event on the agenda of the next available convened IRB meeting for review.

The IRB member (Reviewer) presents the unanticipated problem to the convened IRB for discussion and possible action(s). See Section 1.3 of this policy for possible actions.

Following review, the IRB Administrator updates the database, prints the appropriate letter based upon the Board action, and presents the letter to the IRB Chair for signature. (See Attachment 407-C, Instructions for Unanticipated Problems).

7.2 Review Procedures for Protocol Deviations

If the IRB Chair or designee determines and documents on the protocol deviation report form that the deviation is not an unanticipated problem involving risks to participants or others and the deviation was not a result of serious or continuing noncompliance, the IRB Chair or designee shall complete the review by the expedited review procedure (See Attachment 407-C, Instructions for Unanticipated Problems).

If the IRB Chair or designee determines and documents on the Protocol Deviation Report form that the deviation is an unanticipated problem involving risks to participants or others, the IRB Administrator shall place the deviation report on the agenda of the next available IRB meeting for review.

The IRB Member (Reviewer) presents the protocol deviation to the convened IRB for discussion and possible action(s). See Section 1.3 of this policy for possible actions.

Following review, the IRB Administrator updates the database, prints the appropriate letter based upon the Board action, and presents it to the IRB Chair for signature. (See Attachment 407-C, Instructions for Unanticipated Problems.)

7.3 Reporting Requirements for Unanticipated Problems Involving Risks to Participants or Others, and Protocol Deviations

If the IRB determines that an event is an unanticipated problem involving risks to participants or others, the IRB staff forwards a copy of the report and the IRB letter to the Director of HRPP for reporting to regulatory agencies and institutional officials per SOP 308, Reporting to Regulatory Agencies and Institutional Officials.

APPROVED BY: _____ **DATE:** 09/01/2009

NEXT ESTABLISHED REVIEW DATE: May 2012