

PARTNERS HUMAN RESEARCH COMMITTEE POLICIES AND PROCEDURES

Prompt Reporting of Unanticipated Problems Involving Risks to Subjects or Others

PURPOSE

The purpose of this policy is to define the requirements for prompt reporting to the Partners Human Research Committees (PHRC) of any unanticipated problems involving risks to subjects or others.

This policy is established to comply with Department of Health and Human Services (DHHS) regulations at 45 CFR 46.103(b)(5) and 45 CFR 46.108(a) requiring IRBs to have “written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the Department or Agency head of any unanticipated problems involving risks to subjects or others.” The Food and Drug Administration regulations include the same requirement [21 CFR 56.108(b)(1)].

Additionally, federal regulations 45 CFR 46.113 and 21 CFR 56.113 state, “IRBs shall have the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB’s requirements or has been associated with unexpected serious harm to subjects.” To exercise this important authority in a timely manner, IRBs must be informed promptly of any problem that is unexpected and related (or possibly related) to participation in the research, and that places subjects or others at greater risk of harm than was previously known or recognized. Therefore, once the research is approved by the PHRC, investigators covered by this policy are required to report unanticipated problems to the PHRC, as described in this document.

SCOPE

All investigators conducting non-exempt human research who rely on the PHRC for IRB review are subject to this policy.

UNANTICIPATED PROBLEMS

Although federal regulations require prompt reporting to the IRB of *any unanticipated problems involving risks to subjects or others*, the phrase is not defined in either HHS or FDA regulations. In January 2007, the Office for Human Research Protections (OHRP) released new guidance to assist IRBs in fulfilling this requirement. According to the guidance document OHRP considers *unanticipated problems*, in general, to include any incident, experience, or outcome that meets **all** of the following criteria:

- (1) 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;

- (2) related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- (3) suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Adverse Events

When the incident, experience, or outcome involves any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, the incident is considered an adverse event and is subject to the PHRC Adverse Event Reporting Policy.

Other Incidents, Experiences or Outcomes

Not all incidents, experiences or outcomes involving harm to subjects are adverse events. Some incidents involve social or economic harm, rather than physical or psychological harm. When such incidents occur, the investigator is responsible for assessing whether the incident, experience, or outcome: (1) is unexpected; (2) is related or possibly related to participation in the research; and (3) suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Examples of other incidents, experiences, or outcomes that may meet the definition of unanticipated problems involving risks to subjects or others include:

- Participant complaints
- Laboratory errors
- Medication errors
- Procedural errors
- Unauthorized disclosure of confidential information
- Lost or stolen confidential information
- Disqualification of investigators
- Suspension of investigators

ASSESSING INCIDENTS, EXPERIENCES OR OUTCOMES

Determining whether a particular incident, experience, or outcome is unexpected and whether it is related or possibly related to participation in the research may be difficult. When making this assessment, the investigator should take into consideration whether substantive changes in the research protocol or informed consent document, or other corrective actions may be warranted in order to protect the safety, welfare, or rights of subjects or others. Generally, when substantive changes are proposed to minimize the risk of harm to subjects, the problem is considered an

unanticipated problem involving risks to subjects or others that requires prompt reporting to the PHRC.

For examples of unanticipated problems that do not involve adverse events and need to be reported under the HHS regulations at 45 CFR 46, refer to Appendix B of the OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events.

REQUIREMENTS FOR PROMPT REPORTING OF UNANTICIPATED PROBLEMS

Serious Unanticipated Problems Involving Risks to Subjects or Others

All unanticipated problems involving risks to subjects or others that are **serious** must be reported to the PHRC as soon as possible, but in no event later than 10 working days/14 calendar days of the date the investigator first becomes aware of the problem or event.

Serious unanticipated problems are those incidents, experiences, or outcomes that place subjects at increased risk of serious physical or psychological harm, (e.g., events that result in death; a life-threatening experience; inpatient hospitalization or prolongation of hospitalization; disability or incapacity; congenital anomaly/birth defect; or any other event that may jeopardize the subject's health and may require medical or surgical intervention to prevent one of these outcomes); or any significant economic or social harm (e.g., events that result in criminal or civil liability, damage to financial standing, employability, insurability, reputation, or are stigmatizing).

Note: Changes made in approved research to eliminate an apparent immediate hazard to subjects must be reported within 24 hours.

Unanticipated Problems Involving Risks to Subjects or Others that are Not Serious

All unanticipated problems involving risks to subjects or others that are **not serious** must be reported to the PHRC within 20 working days/30 calendar days of the date the investigator first becomes aware of the problem or event.

For reporting purposes, investigators are asked to complete and submit the PHRC Unanticipated Problem Form. When as a result of the problem, changes are proposed to the research protocol and/or the informed consent document, investigators are also asked to complete and submit the PHRC Amendment Form together with the Unanticipated Problem Form.

REQUIREMENTS FOR REPORTING UNANTICIPATED PROBLEMS AT CONTINUING REVIEW

At continuing review, the PHRC must ensure that the criteria for IRB approval under HHS regulations at 45 CFR 46.111 and, when applicable, FDA regulations at 21 CFR 56.111 continue to be satisfied. Investigators will be asked to provide a summary of any unanticipated problems that occurred since the last IRB review.