Procedure Title: Required Reporting: Unanticipated Problems and Adverse Events

Associated Policy:	Human Research Protection Policy (OSA Policy 1.0)		
Responsible Unit:	Office of Scholarly Activity		
Created:	06/03/2020	**Executive Lead:**	Chief Research Officer
Effective:	06/30/2020	**Revision History:**	.00 – 06-03-2020; .01 – 1-25-2023; .02 – 4-2-2024
Approved by:	Institutional Review Board		
Procedure Number:	134.02		
Key Words:	Adverse Event, Corrective and Preventative Action Plan (CAPA), Reportable Event, Serious Adverse Event, Unanticipated Problems		
Purpose:	To meet the responsibilities for protecting human subjects as issued by the Office for Human Research Protections (OHRP) requirement for individuals involved in the conduct or review of human subjects research at institutions holding OHRP-approved Federal Wide Assurances (FWAs)		

Process:
This SOP serves to inform all agents, offices, departments, and affiliate sites of PNWU regarding reportable events in human subjects research.

This SOP must be used as a guide in parallel with OSA Policy 1.0 to comply with proper reporting of unanticipated problems involving risk to subjects or others. SOPs are not intended to supersede existing institutional policies, and local, state, and federal laws and regulations.

General Information:
Investigators must report all unanticipated problems and events to the IRB. Unanticipated problems or unanticipated problems involving risks to subjects or others include any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected (unforeseen by the investigator or research participant) in terms of nature, severity, or frequency given (a) the research procedures described in the protocol, informed consent document, and (b) the subject population being studied; and
- Related or possibly related to the subject's participation in the research, or if the event or problem possibly or definitely affects the safety, rights, and welfare of current participants; and
- 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.

Using the criteria above, investigators must consider each problem, event, or new information and decide whether or not it represents an unanticipated problem. The IRB needs information about these events and/or problems in order to determinate that (a) risks to participants are minimized, and (b) the risks are reasonable in relation to the anticipated benefits.

Responsible Parties

The Institutional Review Board (IRB) is responsible for:

- Reviewing reportable events in a timely fashion.
- Being a steward of a research environment that promotes the responsible conduct of research;
- Determining whether the reported event meets the threshold of an unanticipated problem involving risk to subjects or others; and

The Office of Scholarly Activity (OSA) is responsible for:

- Fostering a research environment that promotes the responsible conduct of research;
- Providing the necessary support to investigators and the IRB.
- Supporting investigators in helping submit reportable events.
- Developing written policies and procedures for addressing reportable events.
- Monitoring compliance with this SOP.
- Posting this SOP for the PNWU community.

The Investigator is responsible for:

- Documenting and reporting unanticipated problems in a timely manner.
- Assessing unanticipated problems.
- Communicating with the IRB chair, IRB administrator, and OSA staff in a timely fashion,
- Seeking support from OSA and the IRB on proper reportable event submission and any necessary protocol revision.

Definitions

Please reference the Glossary for complete definitions of the following terms and additional terms not listed.

- Adverse Device Effect
- Adverse Events
- Adverse Finding/Reactions
- Clinical Trials of Investigational Medicinal Products (CTIMPs)
- Corrective And Preventive Action (CAPA) Plan
- Federal wide Assurance
- Institutional Review Board (IRB)
- Institutional Official (IO)
- Reportable Event
- Serious Adverse Events
- Suspected Serious Adverse Reactions
- Suspected Unexpected Serious Adverse Reactions
- Unanticipated Problems

Assessment and Reporting of Unanticipated Problems (including Adverse Events):

1. The principal investigator (PI) is responsible for reviewing incidents, problems, events, experiences, or outcomes and determining whether they represent unanticipated problems.
2. Investigators and their study staff are responsible for reporting unanticipated problems via the IRB electronic system **within 10 business days of discovery**.
3. Adverse events that are unanticipated in nature, severity, or duration AND meet any of the following criteria are considered to be serious adverse events and must be reported in the electronic IRB system **within 7 days of discovery**:

a. Results in death; or
b. Is life threatening; or places the subject, in the view of the investigator, at immediate risk of death from the experience as it occurred (this does not include an adverse experience that, had it occurred in a more severe form, might have caused death); or
c. Requires hospitalization or prolongation of existing hospitalization; or

Note: hospitalization is defined as an inpatient admission, regardless of length of stay, even if the hospitalization is a precautionary measure for continued observation. Therefore, participants do not need to be hospitalized overnight to meet the hospitalization criteria. Hospitalization (including hospitalization for an elective procedure) for a preexisting condition (prior to study entry) which has not worsened does not constitute a serious event.

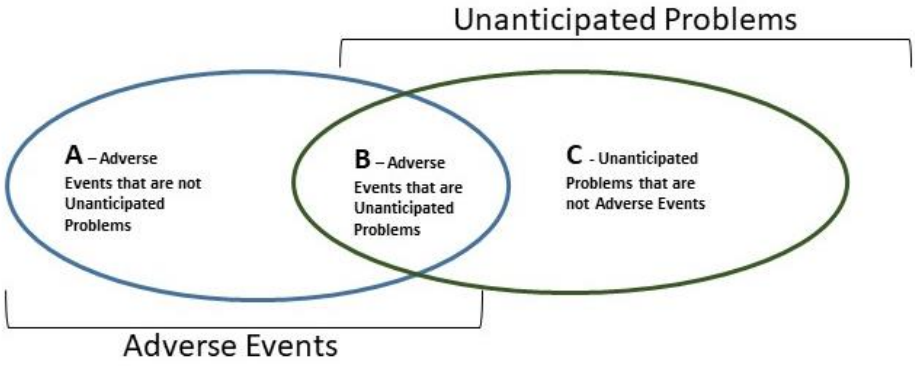
d. Results in persistent or significant disability or incapacity; or substantial disruption of one's ability to conduct normal life functions; or
e. Consists of a congenital anomaly or birth defect in offspring of subjects or their partners taking the investigational medicinal product regardless of time of diagnosis.

4. The event report shall include a corrective and preventative action plan (CAPA). The CAPA plan must address what will be done to correct the problem and prevent future occurrences.
5. The event report shall include a copy of the study event reporting log. Anyone who is not a member of the research team may report concerns of possible unanticipated problems to the IRB chair, institutional official, IRB Administrator, or via the PNWU confidential reporting form on the Office of Compliance, Ethics, and Integrity Services' webpage. In such cases, the reporting party is responsible for making these reports.
6. If an individual, whether investigator, study staff, study participant, or other, is uncertain there is an unanticipated problem to report, he or she may contact the IRB chair or IRB Administrator, to discuss the situation informally and receive guidance as to whether or not the event is reportable.

Examples of Potential Unanticipated Problems:

1. A breach of confidentiality or privacy that involves real or potential risks (e.g., unauthorized use or disclosure of protected health information or a lost/stolen laptop or other electronic device)
2. Complaints from participants or others involved in the research that indicate unexpected risks
3. Data and safety monitoring reports that indicate that the frequency of the magnitude of harms or benefits may be different than initially presented to the IRB
4. Incarceration of a subject in a study not approved to enroll prisoners
5. Identification of information that shows that the risks or potential benefits of the research may be different than initially presented to the IRB
7. Adverse events, adverse reactions, and adverse device effects
8. Warning or determination letters issued by any regulatory body (e.g., FDA, OHRP, DHHS) or funding agency.

NOTE: Adverse events that do not meet the definition of unexpected problems do not need to be reported immediately to the IRB. Instead these may be reported as soon as the investigator is able or no later than at the time of continuing review OR annual check-in. Investigators must track adverse events in order to determine that they are not occurring more frequently than expected and that the events are not more severe than expected.



A - Report as soon as able but no later than annual continuing review
B – Report within 7 business days of discovery if serious, not serious report within 10 business days
C – Report within 10 days

Adapted from the image in the HHS Guidance for Unanticipated Problems and Adverse Events. https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html

IRB Procedures for Unanticipated Problems:

1. Upon receipt of the event report, the IRB Administrator pre-reviews the submission within ten (10) working days. If needed, the IRB Administrator contacts the investigator for corrections, clarifications, or additional information. If the information suggests that subjects may be at risk of harm without immediate intervention, the IRB chair, and the IO will be notified so that necessary steps can be taken to ensure the safety of subjects or investigate the event. The IO and IRB chair have the authority to suspend the study should the need arise.
2. If someone other than the investigator filed the report, a written report summarizing the available information will be developed by the IRB chair or their designee (e.g., the institutional official (IO), IRB administrator, member of the IRB, or assigned staff). The IRB administrator will upload the written summary into the IRB electronic system.
3. The IRB chair, vice chair, or designated reviewer receives and reviews the event report. If needed, the reviewer may request additional information from the investigator or others. The reviewer confirms that the event constitutes an unanticipated problem. If the reviewer feels that study subjects may be at risk of harm without immediate intervention, the IRB chair will be notified. When circumstances warrant, the IRB chair or IO have the authority to suspend the study to protect human subjects.
4. If the IRB chair, vice chair and/or designee determines that the event did not meet the definition of a reportable event, the IRB designee will return the event to the PI with notification that "no action is needed."
5. If the event meets the definition of a reportable event, the IRB chair, vice chair, and/or designee will review the report to determine if it meets the definition of an unanticipated problem involving risk to participants or others. The IRB may take the following actions:

    a. Accept report with no additional requirements.
    b. Approve investigator's proposed change.

c. Place an administrative hold on the study pending IRB receipt of further information from the PI in a time period not to exceed 90 days
d. Conclude that the event meets the definition of noncompliance (e.g., protocol deviation, protocol violation) and request additional information from the study team or require further actions such as, but not limited to, requiring additional training of members of the study team
e. Require a full board review at a convened meeting. The institutional official (IO) may determine this action at any time.
f. Require modification of the protocol
g. Require modification of the consent form or information disclosed during the consent process.
h. Require the study team to provide additional information to current participants. The information may relate to the participant's willingness to continue participation
i. Require that arrangements are made for clinical care outside the research or additional follow-up for participants
j. Require the study team to provide additional information to past participants
k. Require re-consent of current study participants.
l. Alter the frequency of continuing review.
m. Observe the research or the consent process.
n. Determine whether the IRB-approved informed consent form requires revision based on the information about the unanticipated problem
o. Notify investigators at other sites.
p. Obtain additional information.
q. Terminate or suspend the research; if this action is taken, the IRB chair will notify the IO to initiate any reporting actions; if the IRB does not consider the event to represent an unanticipated problem involving risks to participants or others, no further action is required.

6. Reportable events that are not reviewed by the full board will be summarized and reported to the members of the IRB at the next scheduled meeting.

7. If the study is federally funded (e.g., HRSA, OHRP, NIH), the IRB will report the unanticipated problem to the Institutional Official. When required, the institutional official will report the unanticipated problem to the funding agency.

References:

1. Code of Federal Regulations, Title 45, Public Welfare, Department of Health and Human Services Part 46, Protection of Human Subjects, Revised January 15, 2009, Effective July 14, 2009
2. Department of Health and Human Services, Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection, May 5, 2004.
3. Code of Federal Regulations, Title 42 Policies of General Applicability, Department of Health and Human Services, Part 50 Subpart F – Promoting Objectivity in Research
4. Code of Federal Regulations, the Family Educational Rights and Privacy Act (FERPA), 20 U.S.C. § 1232g; 34 CFR Part 99. https://www2.ed.gov/policy/gen/guid/fpco/ferpa/index.html
5. OSA SOP 104: Scope and Authority of the IRB
6. OSA SOP 124: Review and Approval of Studies
7. OSA SOP 129 Required Reporting: Protocol Violations, Deviations and Noncompliance

Version/ Effective Date	Author	Section Changed & Reason for Revision
.00 / 06-30-2020	C. Case	Original SOP - Per HRP recommendations to separate Unanticipated problems and Noncompliance into two SOP.
.01 / 1-25-2023	C. Case	Note at the bottom of page 3 that covers unexpected problems and reporting at the time of continuing review revised to include reporting at the time of annual check-in for those studies not required to undergo annual continuing review.
.02 / 4-2-2024	J. Simmons	Fixed broken link to PNWU confidential reporting form. Now processed by the Office of Compliance, Ethics, and Integrity Services.

Appendices:
Sample Reportable Event Log