



# STATEMENT OF PRACTICE

## External Adverse Event Reports and Unanticipated Problems

**Effective:** February 18, 2015

### I. STATEMENT OF PRACTICE

UM investigators participating in multi-site trials and those using sponsored agents routinely receive reports of external adverse events. Office of Human Research Protections (OHRP) guidance indicates that individual adverse events should only be reported to investigators at all participating institutions when the sponsor determines that the event meets the criteria for an Unanticipated Problem (UaP)

**Note:** An Unanticipated Problem (UaP) is also known as an Unanticipated Problem Involving Risk to Subjects or Others (UPIRSO).

OHRP recommends that any distributed reports include:

- A clear explanation of why the adverse event or series of adverse events has been determined to be an unanticipated problem

**AND**

- A description of any proposed protocol changes or other corrective actions to be taken by the investigators in response to the unanticipated problem.

Investigators may continue to receive reports that have not been assessed as UaPs by the sponsor. When a UM investigator receives a report of an adverse event that is unexpected and related to an agent or procedure used in the UM study, the UM investigator should review the report and assess whether it meets the criteria for an unanticipated problem. If it does, then it should be reported to the IRB.

**Note:** Many reports labeled “unexpected” will **not** meet the criteria above. It is possible for an external adverse event report from a different study, or use of the agent or procedure in a different population or route of administration, to constitute an unanticipated problem for a UM study. The UM investigator should assess whether or not the information in the report indicates a problem that affects the rights and welfare of UM subjects. If, in the judgment of the UM investigator, it does, then the report should be submitted to the IRB.

If the report does not contain sufficient information for the UM investigator to make the needed assessment AND the source of the report (e.g. the sponsor) did not state the event is an “unanticipated problem” or an “unanticipated adverse device effect,” then submission to the IRB is not required.

Both FDA and the HHS Office of Human Research Protections have stated their expectation that an individual external adverse event will rarely meet these criteria for an unanticipated problem.

### II. IDENTIFYING AN UNANTICIPATED PROBLEM

|                                    |  |
|------------------------------------|--|
| Target: P&G Committee              | File Name: SP.ExternalAdverseEventReportingAndUnanticipated... |
| Distribution: Staff, Board Members | PG Number: NA  |
| Lead(s): Existing Web Guidance     | CP Number:   |
| Approved By: P&G Committee         | Implementation Date:   |
| Approval Date:                     | Page Number: Page 1of 1  |



# STATEMENT OF PRACTICE

## External Adverse Event Reports and Unanticipated Problems

For an event or information to be considered an “unanticipated problem,” three criteria must be met:

- It must be “**unanticipated.**” This means the event is **not** expected in terms of its nature, severity or frequency given the:
  - Procedures described in the study documents (e.g. the application, protocol, data and safety monitoring plan, etc.)
  - Characteristics of the subject population being studied (the traits, behaviors, symptoms, diseases, life experiences, or other qualities typically found in the persons comprising those eligible to participate in the study). A UaP is a problem that was expected by neither the research participants nor the investigators (Note: This is not the same as the FDA definition of "unexpected")
- It must be “**related** to the research.” This means there is a reasonable possibility that the event or information may have been caused by, or is linked in a significant way, to the research. This encompasses all aspects of the research; it is not limited to test agents or procedures. It is also not necessarily limited to actions of the UM investigators (for example, labeling changes in an FDA product or an article about animal research).
- The event or information suggests that the research places subjects or others at **greater risk of harm** than was previously known or recognized. This includes physical, psychological, economic, or social harm:
  - Type 1: Potential harm - **Possibility** that previously unsuspected harm may occur (or may occur at a higher than expected rate) even though no one has yet experienced actual harm.
  - Type 2: Actual harm - Recognized harmful or unfavorable outcome that has actually occurred to a research subject, a set of subjects, another individual being treated in a similar fashion in a relevant non-research setting, or another person connected to the research study

**III. REFERENCES**

1. IRBMED [External UaP Reporting](#)
2. IRBMED [Internal Adverse Event Reporting](#)
3. [U-MIC: Unanticipated Problems Involving Risk to Subjects or Others \(UPIRSOs or UaPs\)](#)

|                                    |  |
|------------------------------------|--|
| Target: P&G Committee              | File Name: SP.ExternalAdverseEventReportingAndUnanticipated... |
| Distribution: Staff, Board Members | PG Number: NA  |
| Lead(s): Existing Web Guidance     | CP Number:   |
| Approved By: P&G Committee         | Implementation Date:   |
| Approval Date:                     | Page Number: Page 1of 1  |