A VA employee becomes aware of a LOCAL DEATH, a LOCAL SAE, or a SERIOUS PROBLEM in VA research that appears to be both UNANTICIPATED (i.e., new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol documents and the characteristics of the study population) and RELATED to the research (i.e., reasonably regarded as caused by, or probably caused by, the research).

The unanticipated related incident involves a LOCAL DEATH. Yes: The individual must ensure IMMEDIATE ORAL NOTIFICATION OF THE IRB and WRITTEN NOTIFICATION WITHIN 5 BUSINESS DAYS. The IRB MUST ALERT ORO (by e-mail or telephone) within 2 BUSINESS DAYS AFTER RECEIVING ORAL NOTIFICATION. The Facility Director and ACOS/R&D must receive notification concurrent with ORO.

The unanticipated related incident involves a LOCAL SAE. Yes: The individual must ensure WRITTEN NOTIFICATION OF THE IRB WITHIN 5 BUSINESS DAYS.

The unanticipated related incident involves a SERIOUS PROBLEM. Yes: REPORTING TO ORO AS A DEATH, SAE, OR PROBLEM IS NOT REQUIRED.*

• The individual must ensure IMMEDIATE ORAL NOTIFICATION OF THE IRB and WRITTEN NOTIFICATION WITHIN 5 BUSINESS DAYS.
• The IRB MUST ALERT ORO (by e-mail or telephone) within 2 BUSINESS DAYS AFTER RECEIVING ORAL NOTIFICATION.
• The Facility Director and ACOS/R&D must receive notification concurrent with ORO.

• WITHIN 5 BUSINESS DAYS after receiving written notification, the IRB Chair or a qualified IRB member-reviewer must DETERMINE and DOCUMENT whether any actions are warranted to eliminate apparent IMMEDIATE HAZARDS to subjects.

• The IRB MUST REVIEW the incident and the determination of the IRB Chair or qualified IRB member-reviewer at its next CONVENED MEETING and must DETERMINE and DOCUMENT that:
  (a) The incident was SERIOUS AND UNANTICIPATED AND RELATED to the research; or
  (b) There is INSUFFICIENT INFORMATION to determine whether the incident was serious and unanticipated and related; or
  (c) The incident was NOT SERIOUS and/or the incident was NOT UNANTICIPATED and/or the incident was NOT RELATED.

• The convened IRB MUST also DETERMINE and DOCUMENT:
  (a) Whether any PROTOCOL OR INFORMED CONSENT MODIFICATIONS are warranted, and if so,
  (b) Whether investigators must NOTIFY or SOLICIT RENEWED/REVISED CONSENT from previously enrolled subjects, and if so, WHEN and HOW consent is to be DOCUMENTED.

• For DEATHs, the IRB must notify the FACILITY DIRECTOR and ACOS/R&D OF ALL DETERMINATIONS WITHIN 5 BUSINESS DAYS.
• For SAEs or PROBLEMS, the IRB must notify the FACILITY DIRECTOR and ACOS/R&D WITHIN 5 BUSINESS DAYS after meeting if:
  (a) ACTIONS were taken to ELIMINATE HAZARDS to subjects, or
  (b) The incident was SERIOUS AND UNANTICIPATED AND RELATED TO THE RESEARCH or there was INSUFFICIENT INFORMATION to make the determination, or
  (c) PROTOCOL OR INFORMED CONSENT MODIFICATIONS were warranted.
• The FACILITY DIRECTOR MUST REPORT the incident to ORO WITHIN 5 BUSINESS DAYS after notification.

• Additional reporting may be required under local SOPs or by external agencies (such as FDA or OHRP) or sponsors. If in doubt, check with the relevant entities.
NOTES

1 For complete details, see 38 CFR 16.103(b)(5)(i); 21 CFR 56.108(b)(1), 312.32(a), & 812.3(s); and VHA Handbook 1058.01 §4g, §4j, §4r, §4t, §4y, & §§6a-6.d. This chart does not cover other reportable situations (e.g., program changes, suspensions/terminations). Also see the following ORO guidance;

   • Examples and a Brief Guide for Reporting Apparently Serious Research Information Security Problems That May Be Reportable to ORO under VHA Handbook 1058.01 (Revised September 14, 2015).

   • Examples and a Brief Guide for Reporting Apparently Serious or Apparently Continuing Noncompliance in Human Research That May Be Reportable to ORO under VHA Handbook 1058.01 (Revised September 14, 2015).

2 Local means occurring at the reporting facility’s own research site(s). (VHA Handbook 1058.01§4g)

3 An SAE is an untoward occurrence in human research that results in death, a life-threatening experience, inpatient hospitalization, prolongation of hospitalization, persistent or significant disability or incapacity, congenital anomaly, or birth defect, or that requires medical, surgical, behavioral, social, or other intervention to prevent such an outcome. (VHA Handbook 1058.01§4r)

4 A serious problem is a problem in human research or research information security that may reasonably be regarded as: (1) Presenting a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research personnel, or others, including their rights to privacy and confidentiality of identifiable private information; or (2) Substantively compromising a facility’s HRPP or research information security program. (VHA Handbook 1058.01§4t)

   Examples of apparently serious problems in human research that may be reportable to ORO include the following:

      (1) Any situation that requires action to prevent an immediate hazard to subjects or others.
      (2) Any serious research-related injury to human research subjects, research personnel, or others.
      (3) Any problem described in a VA Pharmacy Benefits Management alert relevant to local human subjects.
      (4) Any problem described in a Data Monitoring Committee report.
      (5) Any combination of problems that collectively present a genuine risk of substantive harm to the safety, rights, or welfare of human research subjects, research personnel, or others, or substantively compromise a facility’s HRPP.

5 Unanticipated/unexpected refer to an event/problem in human research that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol documents and the characteristics of the study population. (VHA Handbook §4y)

6 A related adverse event (AE, VHA Handbook §4a), death, or problem is one that may reasonably be regarded as caused by, or probably caused by, the research. ([VHA Handbook §4j])