OFFICE OF RESEARCH OVERSIGHT

Reporting Local Deaths, Local Serious Adverse Events (SAEs), and Serious Problems in VA Research[1]

September 14, 2015

A VA employee becomes aware of a LOCAL DEATH,[2] a LOCAL SAE,[3] or a SERIOUS PROBLEM[4] 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)[5] **and RELATED to the research** (i.e., reasonably regarded as caused by, or probably caused by, the research)[6]

The unanticipated related incident involves a **LOCAL DEATH.**

NO

The unanticipated related incident involves a **LOCAL SAE.**

NO

The unanticipated related incident involves a **SERIOUS PROBLEM.**

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.

YES

- The individual must ensure **WRITTEN NOTIFICATION OF THE IRB WITHIN 5 BUSINESS DAYS.**

YES

NO

REPORTING TO ORO AS A DEATH, SAE, OR PROBLEM IS NOT REQUIRED.*

- Report to the IRB per local SOPs.
- Reporting to other entities may be required.

- **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. [(HA Handbook §4j)