DEPARTMENT OF VETERANS AFFAIRS
South Texas Veterans Health Care System
San Antonio, Texas 78229-4404

Research Service Policy Memorandum 11-48

December 13, 2011

RESEARCH STANDING OPERATING PROCEDURES (SOP)
Reporting of Unanticipated Problems Involving Risk to Subjects and Others (UPIRSO), Unanticipated Adverse Device Effects (UADE), and Adverse Events (AE)

1. **PURPOSE:** To outline the procedures for reporting of Unanticipated Problems Involving Risk to Subjects and Others (UPIRSO), Unanticipated Adverse Device Effects (UADE), and adverse events (AE) related to human subjects research studies at the STVHCS.

2. **POLICY:**

a. The monitoring and reporting of UPIRSOs, UADEs, and AEs is a critical component of the Human Research Protection Program (HRPP) at the STVHCS.

b. Congruent with Federal Policy (Common Rule) for the protection of human subjects in research, VA regulations require written procedures for the reporting of UPIRSOs to the IRB. Federal policy, and VA and FDA regulations do not contain explicit requirements for the prompt reporting of adverse events (AE) that do not meet the definition of UPIRSO to the IRB, however, investigators must promptly report Unanticipated Adverse Device Effect (UADE) to the IRB.

c. Definitions:

(1) Adverse event (AE): The STVHCS adheres to the broad definition of AE found in VHA Handbook 1058.1 where an AE is defined as "any untoward occurrence [physical, psychological, social, or economic] in a human subject participating in research" and where "the imminent threat of an AE" is included as a reportable event.

(2) Unanticipated Adverse Device Effect (UADE): See definition in the UTHSCSA IRB glossary at: http://research.uthscsa.edu/irb/GLOSSARY OF OIRB TERMS.doc

(3) Unanticipated Problems Involving Risk to Subjects and Others (UPIRSO): See definition in the UTHSCSA IRB glossary at: http://research.uthscsa.edu/irb/GLOSSARY OF OIRB TERMS.doc

(4) Unexpected death: The STVHCS adheres to the definition of unexpected death found in VHA Handbook 1058.1 where an unexpected death is a death of a research subject in which a high risk of death is not projected, as indicated by the written protocol, informed consent form, or sponsor brochure. This definition does not include deaths associated with a terminal condition unless the research intervention clearly hastened the subject's death. A subject's death that is determined to be clearly not associated with the research is not an "unexpected death" for purposes of this SOP.

3. **ACTION:**

a. **Principal Investigator:**

(1) The Principal Investigator is responsible to review all incidents, experiences, and outcomes that may represent an UPIRSO or UADE; determine whether any reviewed incidents, experiences, and

outcomes represents a possible UPIRSO or UADE; and promptly report possible UPIRSOs and UADEs to the IRB according to the UTHSCSA UPIRSO and UADE Policy (http://research.uthscsa.edu/irb/policy/UPIRSO Policy and Procedure.doc) .

(2) The timeline for reporting UPIRSOs and UADEs by the principal investigator to the IRB is specified in the UTHSCSA UPIRSO and UADE Policy (http://research.uthscsa.edu/irb/policy/UPIRSO Policy and Procedure.doc).

(3) Any AE, or an imminent threat of an AE, that does not constitute an UPIRSO does not need to be reported promptly to the IRB, but is summarized and reported to the IRB during Continuing Review.

(4) Any unexpected death of a research subject must be reported promptly to the IRB as specified in the UTHSCSA UPIRSO and UADE Policy (http://research.uthscsa.edu/irb/policy/UPIRSO Policy and Procedure.doc).

b. **IRB:**

(1) The IRB will receive, review, and make a determination whether a Report of Possible UPIRSO or UADE meets criteria as an UPIRSO or UADE.

(2) UPIRSOs or UADEs will be reported as soon as possible, but no later than 48 hours by the IRB via encrypted email or phone, with follow-up paper copy, to the ACOS for R&D, or his/her designee. The IRB will submit a report to the STVHCS within 30 days from the date of determination of resolution of the UPIRSO or UADE.

(3) Unexpected deaths will be reported by the IRB to the ACOS for R&D so that a written report can be submitted by the STVHCS Director to the Office of Research Oversight within 24 hours after the IRB's determination that the death was unexpected or within 5 business days if the IRB has not yet made a determination about whether the death was unexpected.

c. **ACOS for R&D:**

(1) If the ACOS for R&D becomes aware of an UPIRSO or UADE, either directly through the PI or any other component of the STVHCS HRPP, that has not been reported to the IRB, the Principal Investigator will be informed of the requirement to promptly notify the IRB. The ACOS for R&D will also promptly report the possible UPIRSO or UADE to the IRB.

(2) Reports of UPIRSOs and UADEs received by the ACOS for R&D, or his/her designee, will be reported promptly to the Medical Center Director and other institutional officials as described below:

(a) If the report identifies any real or suspected unauthorized use, loss, or disclosure of individually-identifiable information related to a VA research protocol, the ACOS for R&D or designee will then promptly notify the STVHCS Privacy Officer of the breach of confidentiality or privacy.

(b) If the report identifies any compromise of VA information Security, or any real or suspected violation of Information Security requirements related to a VA research protocol, the ACOS for R&D, or designee, will then promptly notify the STVHCS Information Security Officer of the compromise of VA information Security.

(3) The ACOS for R&D will ensure that external regulatory and oversight agencies are notified of UPIRSOs and UADEs as required.

(a) UPIRSOs and UADEs involving VA research will be reported by the IRB to the STVHCS Director to the Office of Research Oversight (ORO) within 5 business days of the IRB's determination that a Report of Possible UPIRSO or UADE meets criteria as an UPIRSO or UADE. This includes UPIRSOs or UADEs that occur at the local institution, and locally-determined UPIRSOs or UADEs based on information received from outside the VA, such as external adverse event reports, new publications, data and safety monitoring reports. The STVHCS Director will notify ORO within 5 business days of being notified of the event/determination. This notification will include the official correspondence from the IRB, and will include the following information when not already included in the IRB correspondence:

1. The nature of the event (UPIRSO or UADE)

2. Name of the institution conducting the research.

3. Title of the research project or grant proposal in which the problem occurred.

4. Name of the principal investigator on the protocol.

5. Identification numbers of the research project as assigned by the UTHSCSA IRB and the STVHCS R&D Office and the identification number of any applicable federal award(s), grant, contract, or cooperative agreement.

6. A detailed description of the problem including the findings of the organization and the reasons for the R&D Committee and/or IRB's decision.

7. Actions that the UTHSCSA IRB has taken or plans to take to address the problem (e.g., requirement to revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.).

8. Additional actions that the STVHCS R&D Committee has taken or plans to take to address the problem (e.g., requirement to revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.).

9. Plans, including a timetable for completion of the investigation and/or corrective action if appropriate, for the UTHCSA IRB to send a follow-up or final report.

10. Plans, including a timetable for completion of the investigation and/or corrective action if appropriate, for the STVHCS R&D Committee to send an additional follow-up or final report.

(b) UPIRSOs or UADEs involving a violation of information security requirements will also be reported by the STVHCS ISO to the VHA Information Security Officer (ISO) within 59 minutes of the STVHCS ISO receiving the notification.

(c) UPIRSOs or UADEs involving real or suspected unauthorized use, loss, or disclosure of individually-identifiable information related to a VA research protocol will be reported by the STVHCS Privacy Officer through the Privacy Violation Tracking System to the VHA Privacy Officer within one hour of the STVHCS Privacy Officer receiving notification.

(d) UPIRSOs or UADEs involving a VA-funded research protocol will also be reported to the VA Office of Research and Development (in addition to the report to ORO) within 10 days of the IRB's determination that a Report of Possible UPIRSO or UADE meets criteria as an UPIRSO or UADE.

(e) Reporting to non-VA regulatory agencies such as the Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA) if the protocol involves a FDA regulated activity, and/or any other federal agencies overseeing research that require separate reports from OHRP will be accomplished by the UTHSCSA IRB according to the procedures and timelines outlined in "IRB Reporting to Internal and External Entities Policy and Procedure" (http://research.uthscsa.edu/irb/policy/Reporting Policy and Procedure.doc). In addition to the UTHSCSA IRB reporting to the above agencies, the STVHCS Medical Center Director will also forward the report, prepared by the UTHSCSA IRB, with a cover letter to the non-VA federal agencies according to the same timelines outlined in the "IRB Reporting to Internal and External Entities Policy and Procedure".

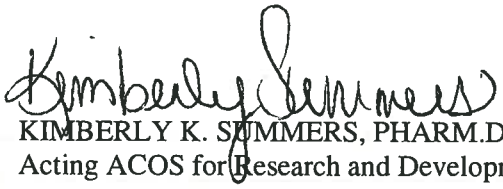
(f) Reports to regulatory agencies by the STVHCS or the UTHSCSA IRB will be copied to the reciprocal office.

4. **REFERENCES:** MOU; VHA Handbook 1200.5; What to Report to ORO

5. **RESPONSIBILITY:** Associate Chief of Staff for Research (151)

6. **RECISSIONS:** Research Service Policy Memorandum 10-48; dated January 20, 2010

7. **RECISSION:** This policy will expire December 2016



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