VA IRB POLICY, ANALYSIS, AND REPORTING FORM FOR SERIOUS ADVERSE EVENTS, SERIOUS PROBLEMS, PROTOCOL DEVIATIONS, AND OTHER REPORTABLE EVENTS TO PARTICIPANTS AND OTHERS IN HUMAN SUBJECTS RESEARCH

09/12/2019

Note: All study staff are advised to err on the side of caution when determining whether an incident is reportable. Consultation with IRB coordinator is urged if any uncertainty exists.

I. Definitions

A. **Adverse Event.** An Adverse Event (AE) is any untoward physical or psychological occurrence in a human subject participating in research.

B. **Serious Adverse Event.** A Serious Adverse Event (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.

C. **Serious Problem**. A serious problem is a problem in human research or research information security that may reasonably be regarded as: 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 substantively compromising a facility's HRPP or research information security program.

D. **Related AE, Death, or Problem.** A related AE, death, or problem is an AE, death, or problem that may reasonably be regarded as caused by, or probably caused by, the research.

E. **Unanticipated and Unexpected.** Unanticipated and unexpected refer to an event or 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.

II. Investigator Reporting Requirements

A. Local Research Deaths

VA personnel, including WOC and IPA appointees, must **IMMEDIATELY** call the IRB Coordinator when they become aware of any local research death that is **BOTH RELATED and UNANTICIPATED,** or possibly related to the research. If the study is under the VA Central IRB, then reporting should be done to the VA Central IRB, however a copy of the report should be immediately conveyed to the local IRB office as well. Within 5 days, written notification must be submitted to the IRB. The IRB is required to alert ORO by e-mail or telephone within 2 business days after being notified of such event and forward concurrent notification to the facility Director and ACOS/R&D. Within 5 business days of written notification, IRB Chair/member must determine and document whether actions are warranted to eliminate apparent immediate hazards to subjects. The IRB must determine/document at next convened meeting that the death was or was not **RELATED and UNANTICIPATED** to the research or if there is insufficient information to make a determination: whether modifications are warranted; and whether/when/how investigators must notify or solicit renewed consent from enrolled subjects. The IRB must notify the Facility Director within 5 business days of determination. The Facility Director must report to ORO within 5 business days after notification.

B. Local Serious Adverse Events and Serious Problems (see definition above and Appendix A for examples)

VA personnel, including WOC and IPA appointees, must submit written notification to the IRB within 5 business days of the discovery of any SAE, event, problem or information that involves VA research locally and is both **RELATED and UNANTICIPATED,** or possibly related to research. The IRB Chair/member is required to review within 5 business days of notification and must also be reviewed by convened IRB as described above. The IRB must notify the Facility

Director and ACOS/R within 5 business days of determination. The Facility Director must report to ORO within 5 business days after notification.

C. Reporting to VA Central IRB and VAAAHS ACOS/R – using cIRB forms 119 and/or 129

In cases where the following are **UNANTICIPATED** and **RELATED** to a research study overseen by the VA Central IRB, reports must be, in writing, within **five** business days of when they come to light.

1. Serious Adverse Events
2. Adverse Device Effects (*serious adverse effects on health or safety or any life-threatening problem or death caused by, or associated with, a device)*
3. Serious Problems
4. Protocol deviations, violations, or noncompliance

The VA Ann Arbor Healthcare System will work with VA Central IRB to ensure all VA and other Federal reporting requirements are met including, but not limited to, those specified in VHA Handbook 1058.01, Reporting Adverse Events in Research to the Office of Research Oversight (ORO).

D. IRB Review of Apparent Serious or Continuing Noncompliance

VA personnel, including WOC and IPA appointees, must ensure that the IRB is notified, in writing, within 5 business days of becoming aware of any apparent serious or continuing noncompliance with IRB or other human research protection requirements. The convened IRB must review any such notifications at the earliest practicable opportunity, not to exceed 30 business days after the notification. The IRB must notify the Facility Director and ACOS/R within 5 business days of determination. The Facility Director must report to ORO within 5 business days after notification. If this is determined from an RCO audit, the notification and tracking from the RCO is required. The IRB is responsible for tracking this to the Facility Director Certification.

E. Protocol Deviations

A protocol deviation occurs when, without significant consequences, the activities on a study diverge from the Institutional Review Board-approved protocol, e.g., missing a visit window because the subject is traveling. VA personnel, including WOC and IPA appointees, must provide written notification to the IRB (in Memo Format) within 30 calendar days after becoming aware of any Protocol Deviations. This will require IRB review at the next convened IRB Meeting.

F. Complaints

The principal investigator and the study team must report complaints submitted by participants or non-participants concerning a VA-approved research study to the VA IRB office (in Memo Format) as follows:

a) Serious Complaints or Problems: Any complaints related to the study design or study staff must be reported within 5 business days if the problems are likely to substantially adversely affect any of the following: the rights, safety, or welfare of the research participant, the participant's willingness to continue participation; or the integrity of the research data, including VA information security requirements.
b) Non-Serious Complaints or Problems: Any complaints or problems related to the study design or study staff should be reported within 5 business days if the complaints and/ or problems occur more than once and are causing confusion and/ or concerns.

G. Ongoing reporting of all Serious Adverse Events and Serious Problems

All serious adverse events and problems that involve local VA research, whether or not anticipated and/or related must be reported in tabular form at continuing review. This includes all events/problems previously reported.

Please submit this report within 5 business days to the VA IRB Office.
Send encrypted email to IRB Coordinator or deliver a hard copy. **DO NOT UPLOAD INTO AAROW!**

Appendix A *Examples of Serious Adverse Events and Serious Problems:*

1. Serious adverse events include: death, a life-threatening experience, inpatient hospitalization, prolongation of hospitalization, persistent or significant disability or incapacity, congenital anomaly, or birth defect.
2. A serious adverse event includes the need for medical, surgical, behavioral, social, or other intervention to prevent any of the above.
3. Injuries that require more than minor medical intervention or lead to serious injury.
4. Any unanticipated problem involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research participants, research staff, or others;
5. Any problem reflecting a deficiency that substantively compromises the effectiveness of a facility's human research protection or human research oversight programs.
6. An intentional violation of the IRB-approved protocol that placed participants or others at increased risk.
7. An accidental or unintentional change to the IRB-approved protocol that placed participants or others at increased risk.
8. A change or interruption to the protocol made without prior IRB review due to concerns about the safety, rights, or welfare of subjects, research personnel, or others, to eliminate an apparent immediate hazard.
9. Interim findings and/or a safety monitoring report that indicate an unexpected change to the risks or potential benefits of the research in terms of severity or frequency.
10. Publication in the literature that indicates an unexpected change to the risks or potential benefits of the research.
11. A complaint of a participant (or others) that indicates unexpected risks have occurred or are imminent.
12. In FDA clinical trials, adverse events that are unexpected, and reasonably related to the study treatment or intervention.
13. In FDA clinical trials, any unanticipated adverse device effect occurring during the investigation. [21 CFR 812.150(a)]
14. Unanticipated problems that involve social or economic harm instead of the physical or psychological harm associated with adverse events.
15. A breach of a participant's confidentiality or privacy that involves potential risk to that participant or others.
16. Deviations from VA IRB regulations and policies.
17. Incarceration of a participant in the course of a study.
18. A change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
19. Any VA Pharmacy Benefits Management (PBM) Alerts related to a facility research project.
20. Data Safety Monitoring Reports or other information describing a safety problem that may impact on the risk/benefit ratio should be promptly reported to and reviewed by the IRB.
21. Suspension of enrollment by the study sponsor or any sponsor analysis describing a safety problem. NOTE: Sponsor "AE Reports" lacking meaningful analysis are not considered problems.
22. Any sponsor analysis describing a safety problem for which action at the facility level may be warranted.
23. Any work-related injury to personnel involved in human research requiring more than minor medical intervention or that leads to serious complications or death.

Serious Adverse Event, Serious Problem, Local Research Deaths, and Other Reportable Event Investigator Reporting Form

VA Ann Arbor Healthcare System
Subcommittee on Human Studies (151)

2215 Fuller Rd.
Ann Arbor, MI 48105

Phone: 734-845-3440
FAX: 734-845-3241

PRINCIPAL INVESTIGATOR:	**VA IRB # (4-digit):**
TITLE OF STUDY:	

Investigators may consult with the IRB Coordinator and/ or IRB Chair for assistance in determining which problems must be reported for review on this form.

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1. CHECK-LIST FOR SERIOUS ADVERSE EVENTS, SERIOUS PROBLEMS, or LOCAL RESEARCH DEATH (Please check one):

☐ (1) **Local Research Death.** VA personnel, including WOC and IPA appointees, must ensure oral notification of the Institutional Review Board (IRB) immediately upon becoming aware of any local research death that is BOTH **RELATED** and **UNANTICIPATED** to the research.

☐ (2) **Local Serious Adverse Events.** VA personnel, including WOC and IPA appointees, must ensure written notification of the IRB within 5 business days after becoming aware of any local SAE that is BOTH **RELATED** and **UNANTICIPATED** to the research.

☐ (3) **Serious (or Non-Serious) Problems.** VA personnel, including WOC and IPA appointees, must ensure written notification of the IRB within 5 business days after becoming aware of any serious or non-serious problem that is BOTH **RELATED** and **UNANTICIPATED** to the research.

If you check at least one item in (1)-(3) then this report requires a screening review by a qualified VA IRB member. Please complete the remainder of this form.

Other Reportable Events:

Protocol Deviations. A protocol deviation occurs when, without significant consequences, the activities on a study diverge from the Institutional Review Board-approved protocol, e.g., missing a visit window because the subject is traveling. VA personnel, including WOC and IPA appointees, must provide written notification to the IRB (in Memo Format) within 30 calendar days after becoming aware of any Protocol Deviations. This will require IRB review at the next convened IRB Meeting.

Complaints. The principal investigator and the study team must report complaints submitted by participants or non-participants concerning a VA-approved research study to the VA IRB office (in Memo Format) as follows:

(a) Serious Complaints or Problems:
Any complaints related to the study design or study staff must be reported within 5 business days if the problems are likely to substantially adversely affect any of the following: the rights, safety, or welfare of the research participant, the participant's willingness to continue participation; or the integrity of the research data, including VA information security requirements.
(b) Non-Serious Complaints or Problems:
Any complaints or problems related to the study design or study staff should be reported within 5 business days if the complaints and/ or problems occur more than once and are causing confusion and/ or concerns.

2. INFORMATION ABOUT THE SERIOUS ADVERSE EVENT OR PROBLEM

Date Event or Problem occurred: **Date Information first received:**

Where did the reported event occur?

☐ VA Ann Arbor Healthcare System ☐ Battle Creek VAMC ☐ Saginaw VAMC

☐ Non-VA facility (Specify) or OTHER:

Complete the following if the event or problem involves a subject at the VA Ann Arbor Healthcare System, Battle Creek VA Medical Center, or Saginaw VA Medical Center:

Participant's Study ID: **Participant's Age:**

SSN (last 4 digits): **Date of study enrollment:**

3. INVESTIGATOR ANALYSIS OF EVENT OR PROBLEM

a) Which of the following best describes the type of event being reported?

☐ Death

☐ A life-threatening experience

☐ Hospitalization (for a research participant not already hospitalized)

☐ Prolongation of Hospitalization (for a research participant already hospitalized)

☐ Persistent or significant disability or incapacity

☐ Need for medical, surgical, behavioral, social, or other intervention (to prevent outcomes such as the examples above)

☐ Privacy and/or security incident

☐ Other (specify):

Please Describe the Event or Problem:

Include the location, time of day, what happened, treatment administered, current status of subject or other individual. If the event did not occur at the Ann Arbor VAMC, then you may attach a letter and/or a MEDWATCH Report from the study sponsor.

b) ☐ The event or problem is RELATED to the research protocol. Please explain how is the event is RELATED to the research protocol:

c) ☐ **The event or problem was UNANTICIPATED (not a previously known consequence of the subject's health status or not previously documented in the research protocol, consent form, current investigator brochure, or product labeling). Please explain:**

4. ADDITIONAL DETAILS and INVESTIGATOR ACTIONS PLANNED or TAKEN:

a) Has a Data Safety and Monitoring Board (DSMB) or Data Monitoring Committee (DMC) reviewed the reported event? (Choose one):

☐ N/A; Project does not have a DSMB or DMC.

☐ No, a review has not yet been conducted by the DSMB or DMC.

☐ Yes, a review has been conducted by the DSMB or DMC.

☐ ***Please check this box if the DSMB or DMC report is attached.***

b) Does the project evaluate a drug or device? ☐ YES ☐ NO

If **yes,** Drug/Device Name(s):

Start Date: Stop Date: or ☐ Continuing

Severity of Event: ☐ Mild ☐ Moderate ☐ Severe ☐ Fatal

Recovery: ☐ Complete ☐ Partial ☐ Minimal ☐ None

c) Was the participant withdrawn from the project? ☐ N/A

☐ **Yes, on:** ☐ **No**

d) Is the reported event (check one): ☐ **Resolved,** *or* ☐ **Ongoing?**

e) Has the sponsor been notified of the reported event? ☐ **N/A**

☐ Yes ☐ No If no, why not?

f) What actions (if any) have already been taken to remedy the situation?
Please describe:

g) Were any changes (e.g., protocol change) initiated without IRB approval to eliminate any apparent immediate hazard to the participant?

☐ YES ☐ NO If NO, go to item **(h)**

If YES, describe the change and and wait for VA IRB review & approval.
Please attach two copies of the revised protocol with changes highlighted in one copy.

Please describe:

h) Are changes required in the protocol and/or VA Consent Form? (and Investigational Drug Brochure for FDA Approved Research Studies?)

☐ YES ☐ NO If NO, go to item **(i)**

If YES, you must stop recruiting new subjects and wait for VA IRB review & approval.
If YES, please attach two copies of the revised protocol/Consent Form with changes highlighted in one copy.

i) Should current subjects or other individuals be notified immediately?

☐ YES ☐ NO If NO, go to item (**j)**
If YES, you may begin to notify them without waiting for IRB approval.

j) Should current subjects be asked to sign a revised Consent Form?

☐ YES ☐ NO If NO, go to item **(k)**
If YES, you must not recruit new subjects. You must wait for VA IRB review & approval.

Number of current participants:

k) Should past participants be notified?

Past participants must be notified if they are likely to be at risk even though they may have completed the active phase of the protocol.

☐ YES ☐ NO If NO, go to **Section 5.**

If YES, please submit a letter/memo that will be sent to participants for VA IRB review & approval.

Number of past participants:

5. Principal Investigator Endorsement:

I certify that this report is accurate and complete to the best of my knowledge.

X_____ **X**_____
Principal Investigator Signature **Date**

Please submit this report within 5 business days to the VA IRB Office.

(Send encrypted email to IRB Coordinator or deliver a hard copy. DO NOT upload into AAROW!)

Adverse Event Reporting Flowchart *(VHA Handbook 1058.01§4j §4r, §4t, §4y)*