

Serious Adverse Event Reporting

IRB Education Meeting

April 21, 2015

It All Comes Down to Risk

- **Minimal Risk:** “the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.” (45 CFR 46.102)
- The IRB must assess whether a research project presents *greater than minimal risk*. (This determination is noted in the IRB’s initial approval letter.)
- Only studies determined to be *greater than minimal risk* require SAE reporting to IRB (and others).

This presentation describes reporting requirements for studies that are classified as *greater than minimal risk*.

Definitions are Important...

- **Adverse Event:** An adverse event (AE) in human subjects research is any untoward physical or psychological occurrence in a human subject participating in research.
- **Serious Adverse Event:** A serious adverse event (SAE) is an AE in human subjects 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. An AE is also considered serious when medical, surgical, behavioral, social, or other intervention is needed to prevent such an outcome.

Definitions are Important...

- **Internal/On-site/Local Event:** An event that occurs in a research participant through the reporting individual's own facility (i.e., MVAHCS human research study subjects) – not at other participating study sites.
- **Unexpected (or Unanticipated) Adverse Event:** An AE that is new or greater than previously known, in terms of nature, severity, or frequency of occurrence, as documented in the protocol or other materials approved by IRB. Such materials may include, but are not limited to: the informed consent form, protocol, clinical investigator's brochure, product labeling, and pharmaceutical package inserts.

External (Off-site) SAE Reporting

- External/Off-site/Non-local SAE: all terms to mean SAEs that have occurred in subjects participating at *other* sites in a trial (*not* the MVAHCS investigator's participants).
- These are not reportable to MVAHCS IRB.
- The MVAHCS investigator should review external SAE reports as they are received, and report any concerns to the IRB that would impact the rights or welfare of subjects or others, and/or the scientific validity of the study.
- The IRB does review Data Safety Monitoring Board/Data Monitoring Committee reports, FDA reports and any other safety reports provided to the IRB by the investigator for information that could change the risk/benefit ratio of a protocol.

Internal (On-site) SAE Reporting

- Internal/On-site/Local SAEs: all terms to mean SAEs that have occurred in subjects participating at the MVAHCS site in a trial.
- These are reportable to MVAHCS IRB if they meet the definitions of **Serious and Unanticipated***.
- This might be *in addition* to other applicable reporting requirements (e.g., reporting to the sponsor).
- Do NOT consider the relationship of the event to the study in deciding whether or not to report it.

* *The **unfounded** classification of an SAE as “anticipated” constitutes serious noncompliance.*

MVAHCS SAE Report Form

MINNEAPOLIS VA HEALTH CARE SYSTEM INSTITUTIONAL REVIEW BOARD
Local Serious Adverse Event Report

Was this event **Serious AND Unanticipated**? Yes No **IF NO, STOP HERE!**
This not an IRB-reportable event.

Report Date: Initial Report Follow-up Report

Date of Event:	Subject ID #:	IRB #:	PI:
Study Title:			
Person Completing Form:	Phone #:	Mail Code:	

This section is to be completed for the Initial Report Only:

When did a study team member first become aware of this event? Date:
The initial SAE Report must be submitted to the IRB within 5 business days of this date. If there has been a delay in reporting, please explain the reason:

Diagnosis/Condition that made this a Serious Adverse Event (key words):

Which CATEGORY describes this Serious Adverse Event?

<input type="checkbox"/> Death	<input type="checkbox"/> Hospitalization (initial or prolonged) <small>Emergency room visits that do not result in admission to the hospital should be evaluated for one of these other serious outcomes listed here.</small>
<input type="checkbox"/> Life-threatening	<input type="checkbox"/> Other Serious (Important Medical Events) <small>Report when the event does not fit the other outcomes, but may jeopardize the patient and may require medical or surgical intervention (treatment) to prevent one of the other serious outcomes listed here.</small>
<input type="checkbox"/> Disability or Permanent Damage	
<input type="checkbox"/> Required Intervention to Prevent Permanent Impairment or Damage (Devices)	
<input type="checkbox"/> Congenital Anomaly / Birth Defect	

Full descriptions of these categories are available at: <http://www.fda.gov/safety/medwatch/howtoreport/ucm053087.htm>

Describe the event, including pertinent medical history and treatment:
(Provide a short chronology of events, including when a study drug/device/procedure was initiated, presenting symptoms, pertinent diagnostic tests, medical interventions, response to treatment, current status, and comorbidities. Has a study drug, device or procedure been temporarily or permanently discontinued as a result of this event?)

Outcome of Event: Resolved on (date): Death (date):
 Ongoing (Submit a follow-up report upon resolution.)

In the opinion of the investigator, is this event RELATED to the subject's research participation?
 Related Probably related Possibly related Not related
If the event is thought to be not related, please provide the reason behind this determination:

PI Signature: Date:

For IRB Use Only Subject ID: SAE Event Date:

IRB Reviewer Determination (to be conducted within 5 business days of report to IRB)

Is the event SERIOUS?	<input type="radio"/> Yes <input type="radio"/> No	} If YES to all 3, notify IRB staff immediately.
Is the event RELATED to the research?	<input type="radio"/> Yes <input type="radio"/> No	
Is the event UNANTICIPATED?	<input type="radio"/> Yes <input type="radio"/> No	

If all are YES: Are any actions needed to prevent immediate hazards to subjects?
 Should study activities be suspended? Yes No
 Should subjects be notified? Yes No If YES, how?
 Any other actions:

NOTE: Per VA policy, if all are YES, this event will be reported at the next convened IRB meeting for determination of further actions, if needed.

If any are NO:
 Is any additional information needed? Yes No If YES, provide comments below:

IRB Reviewer: Date:

For events which are serious, unanticipated and related
 The following items should be addressed at the next convened IRB meeting:

1. Is a protocol revision needed?
2. Is a revision to the informed consent form needed?
3. Should existing subjects be re-consented? If YES, how and when should subjects be re-consented (i.e., in person, by mail, next visit)?
4. What documentation of re-consenting is required (i.e., note in CPRS)?
5. If re-consenting is not required, should subjects be notified in some other way (e.g., informational letter)?
6. Should there be a change in the continuing review frequency?

When Are SAEs Reported?

MINNEAPOLIS VA HEALTH CARE SYSTEM INSTITUTIONAL REVIEW BOARD

Local Serious Adverse Event Report

Was this event **Serious AND Unanticipated**? Yes No If NO, STOP HERE!
This not an IRB-reportable event.

Report Date: Initial Report Follow-up Report

Date of Event:	<input type="text"/>	Subject ID #:	<input type="text"/>	IRB #:	<input type="text"/>	PI:	<input type="text"/>
Study Title:	<input type="text"/>						

- Only adverse events occurring at Minneapolis VA that are both **serious** and **unanticipated** need to be reported to the IRB.
- If an adverse event meets these criteria, the event must be reported in writing to the IRB **within five business days of learning of the event**.
- Submit an *Initial Report* to the IRB with the information that is currently available. Additional information can be provided on a *Follow-Up Report*.

Study Team Responsibilities

- Although any study team member can complete this form, the PI is responsible for timely reporting of local unanticipated SAEs to the IRB, and for implementing any actions necessary to prevent an immediate hazard to subjects.
- Immediately notify the PI (or the investigator who is covering for the PI) of a potentially reportable SAE to ensure timely reporting and determination of possible hazards to subjects.

Person Completing Form:

Phone #:

Mail Code:

This section is to be completed for the Initial Report Only:

When did a study team member first become aware of this event?

Date:

The initial SAE Report must be submitted to the IRB within 5 business days of this date. If there has been a delay in reporting, please explain the reason:

SAE Diagnosis/Condition

- **Do not list all of the subject's current conditions or issues** – just the one(s) that made this a Serious Adverse Event (e.g., your subject is hospitalized due to Acute Renal Failure, not for flank pain, elevated creatinine, nausea, or other conditions that would not have necessitated inpatient treatment.)

Diagnosis/Condition that made this a Serious Adverse Event (key words):

Which CATEGORY describes this Serious Adverse Event?

- | | |
|---|--|
| <input type="checkbox"/> Death | <input type="checkbox"/> Hospitalization (initial or prolonged)
Emergency room visits that do not result in admission to the hospital should be evaluated for one of these other serious outcomes listed here. |
| <input type="checkbox"/> Life-threatening | |
| <input type="checkbox"/> Disability or Permanent Damage | |
| <input type="checkbox"/> Required Intervention to Prevent Permanent Impairment or Damage (Devices) | <input type="checkbox"/> Other Serious (Important Medical Events)
Report when the event does not fit the other outcomes, but may jeopardize the patient and may require medical or surgical intervention (treatment) to prevent one of the other serious outcomes listed here. |
| <input type="checkbox"/> Congenital Anomaly / Birth Defect | |

Full descriptions of these categories are available at: <http://www.fda.gov/safety/medwatch/howtoreport/ucm053087.htm>

SAE Category

- Select all categories that apply to the Diagnosis/Condition that is being reported as an Unanticipated Serious Adverse Event.
- Examples of *Other Serious (Important Medical Events)* include:
 - Allergic bronchospasm requiring treatment in an emergency room
 - Serious blood disorders
 - Seizures/convulsions that do not result in hospitalization
 - Development of drug dependence or drug abuse

Which CATEGORY describes this Serious Adverse Event?

- | | |
|---|--|
| <input type="checkbox"/> Death | <input type="checkbox"/> Hospitalization (initial or prolonged)
Emergency room visits that do not result in admission to the hospital should be evaluated for one of these other serious outcomes listed here. |
| <input type="checkbox"/> Life-threatening | |
| <input type="checkbox"/> Disability or Permanent Damage | |
| <input type="checkbox"/> Required Intervention to Prevent Permanent Impairment or Damage (Devices) | <input type="checkbox"/> Other Serious (Important Medical Events)
Report when the event does not fit the other outcomes, but may jeopardize the patient and may require medical or surgical intervention (treatment) to prevent one of the other serious outcomes listed here. |
| <input type="checkbox"/> Congenital Anomaly / Birth Defect | |

Full descriptions of these categories are available at: <http://www.fda.gov/safety/medwatch/howtoreport/ucm053087.htm>

Narrative Description

- Provide a short chronology of events, pertinent diagnostic tests, medical interventions, and response to treatment. Do not paste progress notes or test results from the subject's medical record.
- Has a study drug, device, or procedure been temporarily or permanently discontinued as a result of this event?
- Describe the subject's status at the time of the report, if known.

Describe the event, including pertinent medical history and treatment:

(Provide a short chronology of events, including when a study drug/device/procedure was initiated, presenting symptoms, pertinent diagnostic tests, medical interventions, response to treatment, current status, and comorbidities. Has a study drug, device or procedure been temporarily or permanently discontinued as a result of this event?)

Outcome of Event:

Resolved on (date):

Death (date):

Ongoing (Submit a follow-up report upon resolution.)

PI's Initial Assessment

In the opinion of the investigator, is this event **RELATED** to the subject's research participation?

Related Probably related Possibly related Not related Not assessable at this time

If the event is thought to be **NOT RELATED**, please provide the reason behind this determination:

Related: Based on the investigators' judgment, there is a reasonable possibility that the adverse event may have been caused by the drug, device or intervention.

Possibly Related: The adverse event may have been caused by the drug, device intervention, however there is insufficient information for the investigator to determine if the event is definitively related to the research.

... but the IRB makes the final decision regarding relatedness.

Initial IRB Review

A qualified IRB member-reviewer must review and document their determination within 5 business days of receipt.

For IRB Use Only

Subject ID:

SAE Event Date:

IRB Reviewer Determination (to be conducted within 5 business days of report to IRB)

Is the event SERIOUS?

Yes

No

Is the event RELATED to the research?

Yes

No

Is the event UNANTICIPATED?

Yes

No

} If YES to all 3,
notify IRB staff
immediately.

If all are YES: Are any actions needed to prevent *immediate* hazards to subjects?

Should study activities be suspended?

Yes

No

Should subjects be notified?

Yes

No

If YES, how?

Any other actions:

NOTE: Per VA policy, if all are YES, this event will be reported at the next convened IRB meeting for determination of further actions, if needed.

If any are NO:

Is any additional information needed?

Yes

No

If YES, provide comments below:

IRB Reviewer:

Date:

Potential IRB Determinations

- If the IRB Reviewer determines that the event is SERIOUS, UNANTICIPATED *and* RELATED/POSSIBLY RELATED, the report is reviewed at the next IRB meeting to address the following questions:

For events which are serious, unanticipated and related

The following items should be addressed at the next convened IRB meeting:

1. Is a protocol revision needed?
 2. Is a revision to the informed consent form needed?
 3. Should existing subjects be re-consented? If YES, how and when should subjects be re-consented (i.e., in person, by mail, next visit)?
 4. What documentation of re-consenting is required (i.e., note in CPRS)?
 5. If re-consenting is not required, should subjects be notified in some other way (e.g., informational letter)?
 6. Should there be a change in the continuing review frequency?
- A letter is sent to the PI describing the IRB's determination and any required follow-up actions.

Discussion & Questions

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