



SCHARP

Safety Reporting Essentials for HVTN Trials

Clinical Affairs
Statistical Center for HIV/AIDS Research & Prevention
(SCHARP)





Presentation Goals

- **Review Safety Monitoring process**
- **Review Reactogenicity Reporting**
- **Discuss AE/SAE/EAE Reporting**
- **Review Clinical Query process (and tips to reduce receiving queries!)**

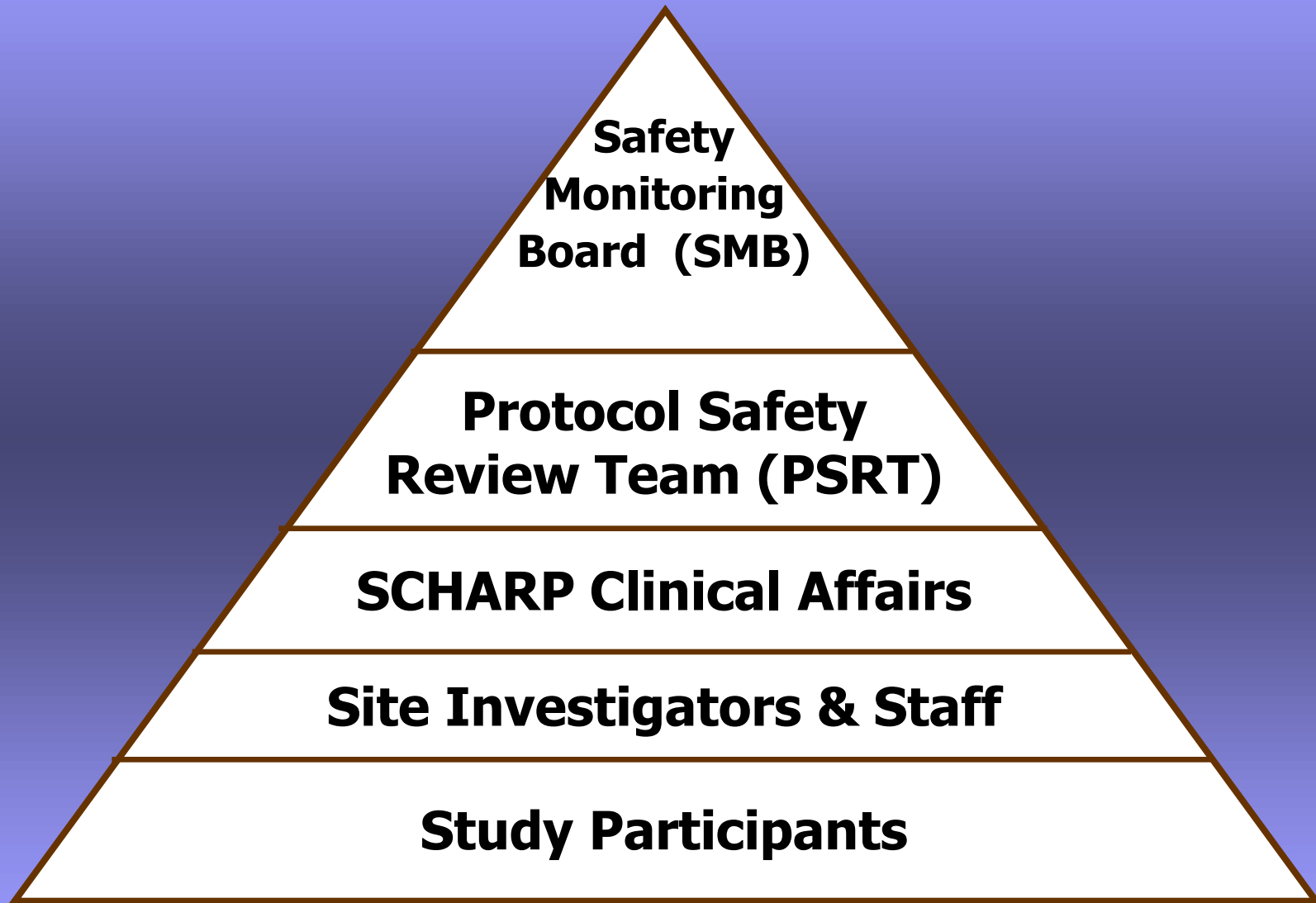


Why do we do safety monitoring?

- **To ensure participant safety:**
 - **HVTN priority, regulatory obligation, and clinical responsibility**
- **To ensure accurate, reliable, and measurable data**
- **To assist in developing safety profiles for the products being tested**



Who is involved in Safety Monitoring?



Study Participants

- **True foundation of HIV research**
- **Source of timely information needed for safety monitoring**
 - **Participants need to know the importance of providing accurate, timely and comprehensive information**





Site Investigators & Staff

- **Evaluate trial participants**
- **Report clinical events to SCHARP, via DataFax, email, and/or telephone**
- **Send Expedited Adverse Event (EAE) reports to DAIDS Safety Office/Regulatory Compliance Center (RCC)**
- **Report AEs as required by local regulatory bodies**





SCHARP Clinical Affairs Safety Associates

- **Serve as link between sites and the Protocol Safety Review Team (PSRT)**
- **Provide timely safety monitoring**
- **Monitor data for unplanned safety pauses**
- **Serve as consultants for clinical safety issues**





Protocol Safety Review Team (PSRT)

➤ **Members:**

Protocol Chair

Co-chair

DAIDS Medical Officer

HVTN Core Medical Monitor

SCHARP Clinical Affairs Safety Associate

Product developer representatives

Clinic Coordinator (may be included)

➤ **Perform regular, systematic review of participant level and summary safety data**





Protocol Safety Review Team (PSRT)

- **Conduct routine safety calls during active phase of study**
- **Review blinded data during unplanned safety pauses to make decisions about the continuation of the trial**



Sources of data included in the safety monitoring process

- **Pre-Existing Conditions**
- **Concomitant Medications**
- **Physical Exams and Vital Signs**
- **Local Laboratory Results**
- **Adverse Experiences**





HVTN Safety Monitoring Board

➤ **Members:**

SMB chair

DAIDS medical officer representative

Non-US representative

US representative

Statistician

Clinician

HVTN director

➤ **Provide routine, unblinded reviews of safety data**

➤ **Perform ad-hoc review of safety data at request of PSRT/FDA**



Key Resources

- **Since each protocol has specific safety requirements (Reactogenicity, AE, and/or EAE reporting), it is crucial to review the following resources:**
 - **“Clinical procedures” & “Safety monitoring and review” sections of the protocol**
 - **“Safety Procedures” section of the protocol-specific VTN Study Specific Procedures (SSP)**
 - **“Safety Monitoring” recorded presentation on the protocol-specific VTN website (under Protocol-specific Training Sessions)**





Reactogenicity Reporting



Reactogenicity Reporting

- **The Reactogenicity reporting interval for most HVTN trials is 3 full days following the day of vaccination.**
- **Local & systemic symptoms that occur during the reactogenicity period should be reported on a Reactogenicity CRF.**
- **If any of these symptoms are \geq Grade 4, they also need to be reported on an AE Log CRF and should be reported as an EAE to RCC/DAERS.**





Reactogenicity Reporting

- Symptoms not listed on the reactogenicity CRF that occur during this 3 day period should be reported on an AE Log CRF.
- AE Log CRFs are also used to report symptoms that have an onset after the reacto reporting period.





Reactogenicity Reporting

The Reactogenicity assessment includes assessment of:

- ▶ Body Temperature
- ▶ Vaccine-related Lesions
- ▶ Proximal lymph nodes
- ▶ Systemic and Local Reactions

<p>1. Was assessment done?..... <input type="checkbox"/> yes <input type="checkbox"/> no → <i>If not done, end of form. Specify reasons in Comments below.</i></p> <p>2. Body Temperature:..... <input type="text"/> <input type="text"/> . <input type="text"/> °C → <i>If ≥ 38.7°C, to be seen by study staff within 48 hours unless improving or resolved.</i></p>	<p>Date of Participant Report</p> <p><input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/></p> <p style="text-align: center;">dd MMM yy</p>																																																																																																		
<p>3. Was right deltoid injected? <input type="checkbox"/> yes <input type="checkbox"/> no → <i>If no, go to item 4.</i></p> <p>3a. Is a vaccine-related lesion visible? <input type="checkbox"/> yes <input type="checkbox"/> no → <i>If no, go to item 4.</i></p> <p>3b. Erythema: <input type="text"/> <input type="text"/> . <input type="text"/> X <input type="text"/> <input type="text"/> cm</p> <p>3c. Induration/swelling/edema: <input type="text"/> <input type="text"/> . <input type="text"/> X <input type="text"/> <input type="text"/> cm</p>	<p>4. Was left deltoid injected? <input type="checkbox"/> yes <input type="checkbox"/> no → <i>If no, go to item 5.</i></p> <p>4a. Is a vaccine-related lesion visible? <input type="checkbox"/> yes <input type="checkbox"/> no → <i>If no, go to item 5.</i></p> <p>4b. Erythema: <input type="text"/> <input type="text"/> . <input type="text"/> X <input type="text"/> <input type="text"/> cm</p> <p>4c. Induration/swelling/edema: <input type="text"/> <input type="text"/> . <input type="text"/> X <input type="text"/> <input type="text"/> cm</p>																																																																																																		
<p>CLINICIAN ASSESSMENT <i>not seen in clinic</i> <i>not assessed</i> <i>not present</i> <i>present</i> → <i>If increased from baseline or previous assessment, complete Adverse Experience Log and state in Comments below. If NOT increased state in Comments below.</i></p>																																																																																																			
<p>5. Axillary Lymphadenopathy: <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/></p>																																																																																																			
<p>SYMPTOMS <i>Instructions: Grade the systemic and local symptoms below according to the DAIDS Table for Grading Severity of AEs.</i></p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 5%;"></th> <th style="width: 15%;">Systemic symptoms:</th> <th style="width: 10%;">none</th> <th style="width: 10%;">mild</th> <th style="width: 10%;">moderate</th> <th style="width: 10%;">severe</th> <th style="width: 10%;">life-threatening</th> </tr> </thead> <tbody> <tr> <td>6.</td> <td>Systemic symptoms:</td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>6a.</td> <td>Malaise and/or fatigue.....</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>6b.</td> <td>Myalgia.....</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>6c.</td> <td>Headache.....</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>6d.</td> <td>Nausea.....</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>6e.</td> <td>Vomiting.....</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>6f.</td> <td>Chills.....</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>6g.</td> <td>Arthralgia.....</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>7.</td> <td>Local symptoms:</td> <td><i>none/NA</i></td> <td><i>mild</i></td> <td><i>moderate</i></td> <td><i>severe</i></td> <td><i>life-threatening</i></td> </tr> <tr> <td>7a.</td> <td>Pain—right deltoid.....</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>7b.</td> <td>Tenderness—right deltoid.....</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>7c.</td> <td>Pain—left deltoid.....</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>7d.</td> <td>Tenderness—left deltoid.....</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </tbody> </table> <p style="text-align: right;">→ <i>To be seen by study staff within 48 hours unless symptoms are improving or have resolved.</i></p>			Systemic symptoms:	none	mild	moderate	severe	life-threatening	6.	Systemic symptoms:						6a.	Malaise and/or fatigue.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	6b.	Myalgia.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	6c.	Headache.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	6d.	Nausea.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	6e.	Vomiting.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	6f.	Chills.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	6g.	Arthralgia.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	7.	Local symptoms:	<i>none/NA</i>	<i>mild</i>	<i>moderate</i>	<i>severe</i>	<i>life-threatening</i>	7a.	Pain—right deltoid.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	7b.	Tenderness—right deltoid.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	7c.	Pain—left deltoid.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	7d.	Tenderness—left deltoid.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Systemic symptoms:	none	mild	moderate	severe	life-threatening																																																																																													
6.	Systemic symptoms:																																																																																																		
6a.	Malaise and/or fatigue.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																																													
6b.	Myalgia.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																																													
6c.	Headache.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																																													
6d.	Nausea.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																																													
6e.	Vomiting.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																																													
6f.	Chills.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																																													
6g.	Arthralgia.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																																													
7.	Local symptoms:	<i>none/NA</i>	<i>mild</i>	<i>moderate</i>	<i>severe</i>	<i>life-threatening</i>																																																																																													
7a.	Pain—right deltoid.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																																													
7b.	Tenderness—right deltoid.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																																													
7c.	Pain—left deltoid.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																																													
7d.	Tenderness—left deltoid.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																																													





Reactogenicity Reporting

- **Although lymphadenopathy is noted to be “present” on the Reactogenicity Form, for safety reporting purposes, severity grading information is taken from the AE Log CRF.**
- **When documenting events of lymphadenopathy on an AE Log CRF, mark “no” in Question #11 – “Was this AE reported on a Reactogenicity form?”**





Reactogenicity Events & EAE Reporting

- **Under the “Standard Level” of EAE reporting, reactogenicity symptoms that meet the criteria for being submitted as an Expedited Adverse Event (EAE) per “*Manual for Expedited Reporting of Adverse Events to DAIDS May 6, 2004,*” include:**
 - ▶ **ALL grade 4 reactogenicity symptoms**
 - ▶ **Other gradeable events, IF they meet EAE criteria**





Adverse Event Reporting



Adverse Event (AE)

“Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product ...does not necessarily have a causal relationship with this treatment...can be any unfavourable or unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not related to the medicinal (investigational) product.”

(International Conference on Harmonization [ICH] E6)



Reporting AEs to SCHARP

- **If you have an event that meets the Protocol’s “Pause Rules” (or you suspect that it might meet one of the pause rules)...**

Call the HVTN Safety Phone

206-786-1343





Reporting AEs to SCHARP

- **After calling the safety phone, send a follow-up email to sc.clin.aff@scharp.org**
 - **Include a description of the AE as well as the site's plan for follow-up and care**





AE CRF – Line 1

HVTN 503 (125) AE-1 (420)

Participant ID: [][]-[4]-[][][][]-[][]
Unit ID Protocol Participant Number Chk

Adverse Experience Log

Date Reported to Site: [][] [][][] [][]
dd MMM yy

1. Adverse Experience (AE) Record diagnosis if available. Include anatomical location, if applicable.

2. Onset Date: [][] [][][] [][]
dd MMM yy

3. Severity

- Grade 1 - Mild
- Grade 2 - Moderate
- Grade 3 - Severe
- Grade 4 - Life-threatening
- Grade 5 - Death

4. Relationship to Study Product

- Definitely related
- Probably related
- Possibly related
- Probably not related
- Not related
Record reason why AE is "not related" in Comments below.

5. Study Product Administration

- No change
- Held
- Permanently discontinued
- N/A

6. Status/Outcome

- Continuing
- Resolved
- Death
- Severity/frequency increased
Report as new AE.
- Continuing at end of study participation

6a. Status/Outcome Date
Leave blank if Status/Outcome is "Continuing."

[][] [][][] [][]
dd MMM yy

7. Treatment *Mark "None" or all that apply.*

- None
- Medication(s)
Report on Concomitant Medications Log.
- New/Prolonged hospitalization
Comment below.
- Procedure/Surgery
Comment below.
- Other
Comment below.

8. Is this AE serious according to ICH guidelines? yes no

9. Has/will this AE be reported as an EAE? yes no

10. Was this AE reported on a Reactogenicity form? yes no

11. This AE was first reported at visit: [][] [][] [][]
Visit code required (regular or interim)

Item 12 is for HIV-infected participants only. For all other participants, go to Comments. not applicable

12. HIV/AIDS event code: [][] OR [][]
Refer to code list on HVTN website.





Adverse Event Log CRF – Line 1

- **Record diagnosis if available**
 - **If a test or procedure was done to confirm the diagnosis, please include this information on the comments line of the AE Log CRF**
- **Include anatomical location if applicable**
- **Do not use abbreviations**
- **Report direction of lab event rather than absolute value**
 - **Elevated ALT (NOT ALT of 63)**
 - **Decreased Hgb**





Participant ID

- 4 - -

Unit ID Protocol Participant Number Chk

Adverse Experience Log

Date Reported to Site

dd MMM yy

1. Adverse Experience (AE)

Record diagnosis if available. Include anatomical location, if applicable.

2. Onset Date

dd MMM yy

3. Severity

- Grade 1 - Mild
- Grade 2 - Moderate
- Grade 3 - Severe
- Grade 4 - Life-threatening
- Grade 5 - Death

4. Relationship to Study Product

- Definitely related
- Probably related
- Possibly related
- Probably not related
- Not related

Record reason why AE is "not related" in Comments below.

5. Study Product Administration

- No change
- Held
- Permanently discontinued
- N/A

6. Status/Outcome

- Continuing
- Resolved
- Death
- Severity/frequency increased
Report as new AE.
- Continuing at end of study participation

6a. Status/Outcome Date

Leave blank if Status/Outcome is "Continuing."

dd MMM yy

7. Treatment Mark "None" or all that apply.

- None
- Medication(s)
Report on Concomitant Medications Log.
- New/Prolonged hospitalization
Comment below.
- Procedure/Surgery
Comment below.
- Other
Comment below.

8. Is this AE serious according to ICH guidelines? yes no

9. Has/will this AE be reported as an EAE? yes no

10. Was this AE reported on a Reactogenicity form? yes no

11. This AE was first reported at visit:

Visit code required (regular or interim)

Item 12 is for HIV-infected participants only. For all other participants, go to Comments.

12. HIV/AIDS event code: OR

not applicable

Refer to code list on HVTN website.





AE: Onset Date – Question # 2

AE Onset Date:

- **Use the date the participant reports the event started.**
- **If the AE is a lab event, the onset date should be the date of the specimen collection (NOT the date the site became aware of the lab results)**





Participant ID

<input type="text"/>	<input type="text"/>	<input type="text"/>	-	4	-	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	-	<input type="text"/>
Unit ID			Protocol		Participant Number				Chk		

Adverse Experience Log

Date Reported to Site

<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
dd		MMM		yy	

1. Adverse Experience (AE)

2. Onset Date

<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
dd		MMM		yy	

Record diagnosis if available. Include anatomical location, if applicable.

3. Severity

- Grade 1 - Mild
- Grade 2 - Moderate
- Grade 3 - Severe
- Grade 4 - Life-threatening
- Grade 5 - Death

4. Relationship to Study Product

- Definitely related
- Probably related
- Possibly related
- Probably not related
- Not related

Record reason why AE is "not related" in Comments below.

5. Study Product Administration

- No change
- Held
- Permanently discontinued
- N/A

6. Status/Outcome

- Continuing
- Resolved
- Death
- Severity/frequency increased
Report as new AE.
- Continuing at end of study participation

6a. Status/Outcome Date

Leave blank if Status/Outcome is "Continuing."

<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
dd		MMM		yy	

7. Treatment Mark "None" or all that apply.

- None
- Medication(s)
Report on Concomitant Medications Log.
- New/Prolonged hospitalization
Comment below.
- Procedure/Surgery
Comment below.
- Other
Comment below.

8. Is this AE serious according to ICH guidelines? yes no

9. Has/will this AE be reported as an EAE? yes no

10. Was this AE reported on a Reactogenicity form? yes no

11. This AE was first reported at visit: Visit code required (regular or interim)

Item 12 is for HIV-infected participants only. For all other participants, go to Comments.

12. HIV/AIDS event code: not applicable





AE: Grading Severity – Question # 3

Severity of the event:

- **Use the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events (December 2004) & the recently distributed Clarification**
 - **Organized by Clinical and Laboratory Events**
 - **Grade 1 – 5 (mild, moderate, severe, life-threatening, death)**
- **If a clinical event is not listed in the Tox Table, sites should use the “Estimating Severity Grade” category on Page 1 of the Tox Table.**





Participant ID

- - -

Unit ID Protocol Participant Number Chk

Adverse Experience Log

Date Reported to Site

dd MMM yy

1. Adverse Experience (AE)

Record diagnosis if available. Include anatomical location if applicable.

2. Onset Date

dd MMM yy

3. Severity

- Grade 1 - Mild
- Grade 2 - Moderate
- Grade 3 - Severe
- Grade 4 - Life-threatening
- Grade 5 - Death

4. Relationship to Study Product

- Definitely related
- Probably related
- Possibly related
- Probably not related
- Not related

Record reason why AE is "not related" in Comments below.

5. Study Product Administration

- No change
- Held
- Permanently discontinued
- N/A

6. Status/Outcome

- Continuing
- Resolved
- Death
- Severity/frequency increased
Report as new AE.
- Continuing at end of study participation

6a. Status/Outcome Date

Leave blank if Status/Outcome is "Continuing."

dd MMM yy

Treatment Mark "None" or all that apply.

- None
- Medication(s)
Report on Concomitant Medications Log.
- New/Prolonged hospitalization
Comment below.
- Procedure/Surgery
Comment below.
- Other
Comment below.

8. Is this AE serious according to ICH guidelines? yes no

9. Has/will this AE be reported as an EAE? yes no

10. Was this AE reported on a Reactogenicity form? yes no

11. This AE was first reported at visit:

Visit code required (regular or interim)

Item 12 is for HIV-infected participants only. For all other participants, go to Comments.

12. HIV/AIDS event code: OR

not applicable

Refer to code list on HVTN website.





AE: Assigning Relationship – Question # 4

Relationship of the event to study product:

- **Refer to the “Manual for Expedited Reporting of Adverse Events to DAIDS, May 6, 2004”**
- **When etiology of the AE is clearly not vaccine related: report as “not related,” i.e., food poisoning, lumbar-puncture-induced headache (alternate etiology must be clearly documented in the site source documents)**



Factors to consider when determining relationship...



- **Pre-clinical and clinical profile of the study products: protocol, package inserts, other published information**
- **Timing of product use relative to onset, resolution, and/or recurrence of the AE**
- **Likelihood of observing the AE in the study population in the absence of product use**
- **Presence of other conditions or exposures that could have caused the AE**
- **Clinical judgment, including judgment of biologic plausibility**





Participant ID

- 4 - -

Unit ID Protocol Participant Number Chk

Adverse Experience Log

Date Reported to Site

dd MMM yy

1. Adverse Experience (AE)

Record diagnosis if available. Include anatomical location, if applicable.

2. Onset Date

dd MMM yy

3. Severity

- Grade 1 - Mild
- Grade 2 - Moderate
- Grade 3 - Severe
- Grade 4 - Life-threatening
- Grade 5 - Death

4. Relationship to Study Product

- Definitely related
- Probably related
- Possibly related
- Probably not related
- Not related

Record reason why AE is "not related" in Comments below.

5. Study Product Administration

- No change
- Held
- Permanently discontinued
- N/A

6. Status/Outcome

- Continuing
- Resolved
- Death
- Severity/frequency increased
Report as new AE.
- Continuing at end of study participation

6a. Status/Outcome Date

Leave blank if Status/Outcome is "Continuing."

dd MMM yy

7. Treatment Mark "None" or all that apply.

- None
- Medication(s)
Report on Concomitant Medications Log.
- New/Prolonged hospitalization
Comment below.
- Procedure/Surgery
Comment below.
- Other
Comment below.

8. Is this AE serious according to ICH guidelines? yes no

9. Has/will this AE be reported as an EAE? yes no

10. Was this AE reported on a Reactogenicity form? yes no

11. This AE was first reported at visit:
Visit code required (regular or interim)



AE: Study Product Administration – Question # 5



- ***No change:*** Mark if the AE does NOT result in a study product hold, permanent discontinuation, or change in administration.
- ***Held:*** Mark if the AE results in a study product hold. If multiple AEs are reported at the same visit, only mark ‘Held’ for the AE(s) that contributed to the product hold.
- ***Permanently discontinued:*** Mark if the AE results in permanent discontinuation of study product. If multiple AEs are reported at the same visit, only mark ‘Permanently discontinued’ for the AE(s) that contributed to the permanent discontinuation.
- ***N/A (not applicable):*** Mark if the AE occurred after the participant had completed all administration of the study product, or the study product is held or permanently discontinued for a different AE or other reason, or the AE is Grade 5-death.





Participant ID

- 4 - -

Unit ID Protocol Participant Number Chk

Adverse Experience Log

Date Reported to Site

dd MMM yy

1. Adverse Experience (AE)

Record diagnosis if available. Include anatomical location, if applicable.

2. Onset Date

dd MMM yy

3. Severity

- Grade 1 - Mild
- Grade 2 - Moderate
- Grade 3 - Severe
- Grade 4 - Life-threatening
- Grade 5 - Death

4. Relationship to Study Product

- Definitely related
- Probably related
- Possibly related
- Probably not related
- Not related

Record reason why AE is "not related" in Comments below.

5. Study Product Administration

- No change
- Held
- Permanently discontinued
- N/A

6. Status/Outcome

- Continuing
- Resolved
- Death
- Severity/frequency increased
Report as new AE.
- Continuing at end of study participation

a. Status/Outcome Date

Leave blank if Status/Outcome is "Continuing."

dd MMM yy

7. Treatment Mark "None" or all that apply.

- None
- Medication(s)
Report on Concomitant Medications Log.
- New/Prolonged hospitalization
Comment below.
- Procedure/Surgery
Comment below.
- Other
Comment below.

8. Is this AE serious according to ICH guidelines? yes no

9. Has/will this AE be reported as an EAE? yes no

10. Was this AE reported on a Reactogenicity form? yes no

11. This AE was first reported at visit: Visit code required (regular or interim)





Participant ID

- 4 - -

Unit ID Protocol Participant Number Chk

Adverse Experience Log

Date Reported to Site

dd MMM yy

1. Adverse Experience (AE)

Record diagnosis if available. Include anatomical location, if applicable.

2. Onset Date

dd MMM yy

3. Severity

- Grade 1 - Mild
- Grade 2 - Moderate
- Grade 3 - Severe
- Grade 4 - Life-threatening
- Grade 5 - Death

4. Relationship to Study Product

- Definitely related
- Probably related
- Possibly related
- Probably not related
- Not related

Record reason why AE is "not related" in Comments below.

5. Study Product Administration

- No change
- Held
- Permanently discontinued
- N/A

6. Status/Outcome

- Continuing
- Resolved
- Death
- Severity/frequency increased
Report as new AE.
- Continuing at end of study participation

6a. Status/Outcome Date

Leave blank if Status/Outcome is "Continuing."

dd MMM yy

7. Treatment Mark "None" or all that apply.

- None
- Medication(s)
Report on Concomitant Medications Log.
- New/Prolonged hospitalization
Comment below.
- Procedure/Surgery
Comment below.
- Other
Comment below.

8. Is this AE serious according to ICH guidelines? yes no

9. Has/will this AE be reported as an EAE? yes no

10. Was this AE reported on a Reactogenicity form? yes no

11. This AE was first reported at visit:
Visit code required (regular or interim)



AE: Seriousness – Question #8

- **Serious Adverse Event (SAE) → Based on the outcome of the AE, regardless of severity or relationship to study product**
- **ICH Guidelines defines an SAE as: Any untoward medical occurrence that, at any dose...**
 - **results in death**
 - **results in persistent or significant disability / incapacity**
 - **is a congenital anomaly / birth defect**
 - **is life-threatening**
 - **requires inpatient hospitalization or prolongation of existing hospitalization**





AE: Expedited Reporting – Question #9

- **Adverse events meeting the criteria for expedited reporting (EAE) must be reported to the DAIDS Safety Office/Regulatory Compliance Center (RCC)/DAERS**
- **The determination of an EAE as described in the “Manual for Expedited Reporting of Adverse Events to DAIDS, May 6 2004” includes these aspects of the event:**
 - Seriousness
 - Severity
 - Relatedness
 - Level of reporting





Reporting EAEs to DAIDS/RCC (DAERS)

- **Report all protocol required EAEs**
- **Report other events that do not meet the protocol required reporting criteria, but are believed to be of sufficient concern by the Investigator, on an expedited basis to DAIDS**
- **Refer to the protocol for instructions on how to submit an EAE to RCC/DAERS**



Standard Level of Adverse Event Reporting



Serious Adverse Events (According ICH guidelines) **	Adverse Event	Relationship to Study Product	AE Log CRF (DataFax to SCHARP)	EAE Form to DAIDS RCC
<p>* Fetal Loss (e.g. spontaneous abortion) may or may not meet criteria to be an SAE according to ICH guidelines. Refer to Section 2.1 "Seriousness" in the <i>Manual for Expedited Reporting of Adverse Events to DAIDS</i> (dated May 6, 2004) for additional details.</p>	Results in Death	Regardless of relationship	YES	YES
	Congenital anomalies, birth defects or fetal loss*	Regardless of relationship	YES	YES
	Results in persistent or significant disability or incapacity	Regardless of relationship	YES	YES
	Requires or prolongs existing hospitalization	All relationships except for "Not Related"	YES	YES
	Requires intervention to prevent significant/permanent disability or death	All relationships except for "Not Related"	YES	YES
	Is life-threatening (including all Grade 4 adverse events)	All relationships except for "Not Related"	YES	YES
	All other SAEs	Not related to study product	YES	NO
Non-serious Adverse Events	All other non-serious AEs	Regardless of relationship	YES	NO



Avoiding reconciliation queries when reporting an EAE

- **AE/EAE reconciliation is performed at SCHARP by Clinical Affairs staff to ensure that events residing in the Clinical data base at SCHARP and the EAE data base at RCC are consistent.**
- **E mail queries are sent to Site staff or RCC requesting data clarification about inconsistencies.**
- **For each EAE reported to RCC/DAERS the HVTU staff must also complete an AE CRF and send it to SCHARP Datafax.**
- **After participant termination, EAES should continue to be reported to RCC/DAERS if sites become aware of an EAE. AEs are not to be reported**





EAE and AE data elements that are compared for consistency/reconciliation

- **Key fields: Network, Protocol, Participant ID**
- **Adverse Experience/Primary AE**
- **Onset date**
- **Severity/Grade**
- **Relationship to Study Product**
- **Reportability – when marked yes, question 9 on the AE CRF identifies that an EAE was sent to the DAIDS Safety Office, RCC/DAERS.**





What triggers a query?

- **An EAE is reported to RCC/DAERS and there is no corresponding AE CRF at SCHARP**
- **An AE is completed and question 9 is marked “yes” but RCC is not reporting an EAE received**
- **AE question 9 is marked “no” but RCC is reporting an EAE**
- **AE and EAE data differences in onset date, grade, relationship, and event (the event terms need to be similar if not exactly the same)**





Clinical Queries



HIV VACCINE
TRIALS NETWORK

SCHARP





What is a Clinical Query?

- **Clinical queries are questions about data sent from the SCHARP Clinical Affairs Staff to the site via e-mail pdf attachments**
- **There are two types of queries that can be sent by Clinical Affairs in the same pdf attachment**
 - ▶ Clinical queries
 - ▶ Adverse Event Clarification Requests



Clinical Queries

- **Generated by SCHARP Clinical Affairs Safety Associates**
- **Request for additional information about an abnormal lab value, physical exam, and/or a clinical adverse event**
- **Often sent in response to Protocol Safety Review Team (PSRT) review**
 - ▶ May include PSRT suggestions or recommendations



Clinical Query

- **Lists the Participant ID and Visit #**
- **Lists the CRF/variable in question**
- **Includes site response line**
 - ▶ Must be filled in by a licensed healthcare provider
- **Includes signature/date line**
 - ▶ Must be signed by a licensed healthcare provider





Responding to Clinical Queries

- **As directed by the query, sites should write their response to the clinical query on the clinical query page, sign & date, then fax to SCHARP Clinical Affairs at (206)667-4812. Please do not use the DataFax #.**
- **If needed, update any related CRFs and fax to SCHARP DataFax.**





AE Clarification Requests

- **Generated by SCHARP Adverse Event coding staff**
- **Prefaced with “AE CLARIFICATION REQUEST” to differentiate between queries about clinical events and queries specific to adverse event clarification.**
- **Include instructions on how to clarify/amend the Adverse Experience Log and do NOT include a site response line**
 - ▶ Site must refax edited AE Log page to SCHARP DataFax





Any Questions?

**Please feel free to e-mail
sc.clin.aff@scharp.org**



**HIV VACCINE
TRIALS NETWORK**