

HPTN 035

Adverse Event Reporting

Anne S Coletti
Family Health International

Definition: Adverse Event

Any untoward medical occurrence in a clinical research participant administered an investigational product and which does not necessarily have a causal relationship with the investigational product.

An AE can therefore be an unfavorable or unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of an investigational product, whether or not considered related to the investigational product.

ICH E6, Glossary 1.2

Definition: Adverse Event

- ◆ For HPTN 035, the ICH definition of adverse event will be applied:
 - To all participants in all four treatment groups
 - Beginning from the time of randomization
- ◆ For HPTN 035, the term “investigational product” in the definition refers to:
 - BufferGel
 - PRO 2000/5 Gel (P)
 - Placebo gel

Definition: Serious Adverse Event

Any untoward medical occurrence that at any dose:

- ◆ *Results in death*
- ◆ *Is life-threatening*
- ◆ *requires inpatient hospitalization or prolongation of existing hospitalization*
- ◆ *Results in persistent or significant disability/incapacity*
- ◆ *Is a congenital anomaly/birth defect*

ICH E6, Glossary 1.50

Definition: Serious Adverse Event

Important medical events that may not be immediately life-threatening or result in death or hospitalization, but may jeopardize the participant or may require intervention to prevent one of the above-listed outcomes, also may be considered serious.

**ICH E2A, Clinical Safety Data Management:
Definitions and Standards for Expedited Reporting**

Definition: Expedited Adverse Event

AE that meets criteria for expedited reporting to DAIDS
(term used for ease of reference, not a “definition” per se)

AE Evaluation and Reporting

- ◆ **All AEs in all treatment groups must be graded for severity and assessed for relationship to study product**
- ◆ **All AEs in all treatment groups must be reported on AE case report forms**
 - **AE term**
 - **Onset date**
 - **Severity**
 - **Relationship to study product**
 - **Study product administration**
 - **Status/outcome and date**
 - **Treatment**
 - **SAE/EAE**

AE Case Report Form

Statistical Center for HIV/AIDS Research & Prevention (SCHARP) **Adverse Experience Log (AE-1)**

SAMPLE: DO NOT FAX TO DATAFAX ■■■■■■■■■■ Note: Number pages sequentially (001, 002, 003) for each participant. Page

HPTN 035 Ph II/III Microbe (013) AE-1 (420)

Participant ID -- **Adverse Experience Log** Date Reported to Site

Site Number Participant Number Chk dd MMM yy

1. Adverse Experience (AE) **2. Onset Date**

Record diagnosis if available. Include anatomical location, if applicable. dd MMM yy

3. Severity **4. Relationship to Study Product** **5. Study Product Administration**

Grade 1 - Mild Definitely related No change

Grade 2 - Moderate Probably related Held

Grade 3 - Severe Possibly related Permanently discontinued

Grade 4 - Life-threatening Probably not related N/A

Grade 5 - Death Not related Change in administration

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

6. Status/Outcome **6a. Status/Outcome Date** **7. Treatment** *Mark "None" or all that apply.*

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

Leave blank if Status/Outcome is "Continuing."

dd MMM yy

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 FDA/ICH guidelines? ^{yes} ^{no}

9. Has this AE been reported to RCC? ^{yes} ^{no}

10. This AE was first reported at visit:

Visit code required (regular or interim).

Comments: _____

27-AUG-04 **SAMPLE**

Language Staff Initials / Date

I:\forms\IPTN_035\forms\std_ph_ae_log_10jun04.fm

Severity and Relationship

Severity

- ◆ Grade 1: Mild
- ◆ Grade 2: Moderate
- ◆ Grade 3: Severe
- ◆ Grade 4: Life-Threatening
- ◆ Grade 5: Death

Based on the DAIDS Table for Grading Adult and Pediatric Adverse Events (TBA Fall 2004)

Relationship

- ◆ Definitely related
- ◆ Probably related
- ◆ Possibly related
- ◆ Probably not related
- ◆ Not Related

Based on the Manual for Expedited Reporting of AEs to DAIDS, IBs, clinical judgement

Relationship

- ◆ **Definitely Related**: AE and administration of study product are related in time, and a direct association can be demonstrated
- ◆ **Probably Related**: AE and administration of study product are reasonably related in time, and AE is more likely explained by study product than other causes
- ◆ **Possibly Related**: AE and administration of study product are *reasonably* related in time, and AE can be explained equally well by causes other than study product

Relationship

- ◆ Probably Not Related: Potential relationship between AE and study product could exist (i.e., the possibility cannot be excluded), but AE is most likely explained by causes other than study product
- ◆ Not Related: AE is clearly explained by another cause not related to study product

Definition: Expedited Adverse Event

AE that meets criteria for expedited reporting to DAIDS

Definition: Expedited Adverse Event

AE that meets criteria for expedited reporting to DAIDS

- ◆ Intensive EAE reporting in Phase II
- ◆ Standard EAE reporting in Phase IIb

- ◆ EAE reporting required through each participant's scheduled duration of follow-up (plus reportable pregnancy outcomes post study exit)

Intensive EAE Reporting

In Phase II, report within 3 business days all AEs that:

- ◆ Result in death
- ◆ Are congenital anomalies, birth defects, or fetal losses
- ◆ Result in persistent or significant disabilities or incapacities
- ◆ Requires or prolong hospitalization, or requires intervention to prevent significant/permanent disability or death, AND are judged definitely, probably, possibly, or probably not related, to study product
- ◆ Are Grade 3 or 4 AEs AND are judged definitely, probably, possibly, and probably not related to study product

Standard EAE Reporting

In Phase IIb, report within 3 business days all AEs that:

- ◆ Result in death
- ◆ Are congenital anomalies, birth defects, or fetal losses
- ◆ Result in persistent or significant disabilities or incapacities
- ◆ Requires or prolong hospitalization, or requires intervention to prevent significant/permanent disability or death, AND are judged definitely, probably, possibly, or probably not related, to study product
- ◆ Are Grade 4 AEs AND are judged definitely, probably, possibly, and probably not related to study product

EAE Reporting

In both Phases II and Phase IIb, additionally report within 3 business days all AEs that:

- ◆ **Are judged definitely, probably, possibly, or probably not related, to study product AND of sufficient concern to be reported on an expedited basis to DAIDS**
- ◆ **Are SAEs not related to study product but could be associated with study participation or procedures**
- ◆ **Are unexpected SAEs judged definitely, probably, possibly, or probably not related, to study product that occur after the protocol-defined EAE reporting period if study staff become aware of their occurrence**

EAE Report Form, Page 1 of 7

Division of AIDS Safety Office EXPEDITED ADVERSE EVENT (EAE) Form

Please type or print in English

To: DAIDS SAFETY OFFICE
Fax: 1-800-275-7619 (USA) or
+ 1-301-897-1710 (International)
Phone: 1-800-537-9979 (USA) or
+ 1-301-897-1709 (International)
Email: RCCSafetyOffice@Tech-Res.com

Sent by: _____
Phone: _____ Fax: _____
E-mail: _____
Date Sent:
D D / M O N / Y Y Y Y
No. of Pages: _____ (Including this cover sheet)
Patient/Volunteer ID Number: _____

REPORTER AND SITE INFORMATION

Site Name: _____ Site Number: _____
Site Awareness Date:
D D / M O N / Y Y Y Y
Site Report Date:
D D / M O N / Y Y Y Y
Reporter Same as Sender? YES NO
If YES, do not repeat contact information provided above.
Reporter Name: _____
Phone: _____ Fax: _____
Email: _____

New Report: (Send all pages of the completed form.)
Follow-up Report: (If Follow-up Report, provide Date of Original Report.) Date of Original Report:
D D / M O N / Y Y Y Y
Pages: 1 2 3 4 5 6 7 ALL (For Follow-up Reports, submit only updated pages. Check all that apply.)

SAFETY OFFICE USE ONLY

Received Date Stamp: _____
AE NUMBER:
PROTOCOL NUMBER(S): _____

EAE Report Form, Page 2 of 7

Patient/Volunteer ID Number: _____

Site Report Date: / /

D D / M O N / Y Y Y Y

Is this a Serious Adverse Event (SAE) as defined in ICH* E6 ? (* International Conference on Harmonisation) YES NO

- Results in death
- Is a congenital anomaly/birth defect
- Results in persistent or significant disability/incapacity
- Is life-threatening
- Requires inpatient hospitalization or prolongation of existing hospitalization

1. PROTOCOL INFORMATION

Protocol Number: _____

- Network Affiliation (check one): None
- AACTG AIEDRP CIPRA CPCRA
- ESPRIT HPTN HVTN IRP
- PACTG SMART Other Network, specify _____

Protocol Number: _____ N/A

- Network Affiliation (check one): None
- AACTG AIEDRP CIPRA CPCRA
- ESPRIT HPTN HVTN IRP
- PACTG SMART Other Network, specify _____

Protocol Number: _____ N/A

- Network Affiliation (check one): None
- AACTG AIEDRP CIPRA CPCRA
- ESPRIT HPTN HVTN IRP
- PACTG SMART Other Network, specify _____

2. SUBJECT INFORMATION For each question below, please check the appropriate box.

- Age:** Days* Months* Years
- Sex at Birth:** Male Female Unknown
- Pregnant:** Yes No Unknown
- (If Yes) Duration _____ week(s)
- Height* :** _____ cm in
- Weight:** _____ kg lb
- Race:** Native American or Alaska Native Asian Black or African American
 Native Hawaiian or Other Pacific Islander Unknown White
 Other, specify _____

EAE Report Form, Page 3 of 7

D D / M O N / Y Y Y Y

3. FOR ALL STUDY AGENTS For therapeutics administered on a cyclic schedule, also complete the Supplemental DAIDS EAE Report Form and check here if attached.

A	Protocol Number					
	Study Agent	Agent 1	Agent 2	Agent 3	Agent 4	Agent 5
B	Generic/INN Name or the Study Agent Name/ Abbreviation as listed in the Protocol. If Combination Agent, use Study Agent name/abbreviation or list individual components.					
C	Dose					
D	Route					

4. FOR STUDY AGENTS OTHER THAN VACCINES OR THERAPEUTIC VACCINES N/A

* C – Continued Without Change; O – Course Completed or Subject Off Study Agent at AE Onset; D – Permanently Discontinued; R – Dose or Schedule Reduced; T – Temporarily Held; U – Unknown

	Study Agent	Agent 1	Agent 2	Agent 3	Agent 4	Agent 5
A	Schedule of Administration					
B	Date of First Dose (DD/MON/YYYY)					
C	Date of Last Dose (DD/MON/YYYY)					
D	Action Taken with Study Agent *					
E	Date of Action Taken with Study Agent (DD/MON/YYYY)					
F	Distributed by DAIDS	Yes <input type="checkbox"/> No <input type="checkbox"/>	Yes <input type="checkbox"/> No <input type="checkbox"/>	Yes <input type="checkbox"/> No <input type="checkbox"/>	Yes <input type="checkbox"/> No <input type="checkbox"/>	Yes <input type="checkbox"/> No <input type="checkbox"/>
	If No, specify manufacturer. If unknown, specify					

EAE Report Form, Page 4 of 7

Patient/Volunteer ID Number: _____

Site Report Date:
D D / M O N / Y Y Y Y

5. FOR VACCINES ONLY (INCLUDING THERAPEUTIC VACCINES) List all dates (DD/MON/YYYY) of vaccine administration. N/A

* C – Continued Without Change; O – Course Completed or Subject Off Study Agent at AE Onset; D – Permanently Discontinued;
 R – Dose or Schedule Reduced; T – Temporarily Held; U – Unknown

<p>a. <small>__ __ / __ __ __ / __ __ __ __</small> <small>D D M O N Y Y Y Y</small></p>	<p>c. <small>__ __ / __ __ __ / __ __ __ __</small> <small>D D M O N Y Y Y Y</small></p>	<p>e. <small>__ __ / __ __ __ / __ __ __ __</small> <small>D D M O N Y Y Y Y</small></p>
<p>b. <small>__ __ / __ __ __ / __ __ __ __</small> <small>D D M O N Y Y Y Y</small></p>	<p>d. <small>__ __ / __ __ __ / __ __ __ __</small> <small>D D M O N Y Y Y Y</small></p>	<p>f. <small>__ __ / __ __ __ / __ __ __ __</small> <small>D D M O N Y Y Y Y</small></p>

Action Taken with Study Agent * (enter code for the vaccine treatment regimen from codes listed above): _____

EAE Report Form, Page 5 of 7

Patient/Volunteer ID Number: _____

Site Report Date: / /
D D / M O N / Y Y Y Y

6. PRIMARY ADVERSE EVENT

PRIMARY AE <small>List only one Primary AE.</small>	Relationship to Study Agent(s) Listed in Section 3 *					Severity Grade of Primary AE	Onset Date <small>(DD/MON/YYYY)</small>	Status Code **	Status Date <small>(DD/MON/YYYY)</small>
	Agent 1	Agent 2	Agent 3	Agent 4	Agent 5				

*** Relationship Code**
 1 – Definitely Related
 2 – Probably Related
 3 – Possibly Related
 4 – Probably Not Related
 5 – Not Related
 6 – Pending (temporary assignment for death)

**** Status Code at Most Recent Observation**
 1 – Recovered / Resolved
 2 – Recovering / Resolving
 3 – Not Recovered / Not Resolved
 4 – Recovered / Resolved with Sequelae
 5 – Death
 6 – Unknown

7. OTHER CLINICALLY SIGNIFICANT EVENTS ASSOCIATED WITH PRIMARY AE None

Other Clinically Significant Events Associated with Primary AE	Severity Grade	Onset Date <small>(DD/MON/YYYY)</small>
1.		
2.		
3.		
4.		

EAE Report Form, Page 6 of 7

Patient/volunteer ID Number: _____

Site Report Date:
D D / M O N / Y Y Y Y

8. RELEVANT LABORATORY TESTS List normal or abnormal tests that help explain the Primary AE. List tests below OR attach copy of test results. None

Test	Collection Date (DD/MON/YYYY)	Result	Units	Lab Normal Range	Lab Value Previous to this AE	Previous Lab Collection Date (DD/MON/YYYY)
1.						
2.						
3.						
4.						

9. RELEVANT DIAGNOSTIC TESTS (NON-LAB) List tests below OR attach copy of test results. None

Test	Test Date (DD/MON/YYYY)	Results/Comments
1.		
2.		
3.		
4.		

10. CONCOMITANT MEDICATIONS List Concomitant Medications being taken at onset of primary AE OR attach copy of concomitant medication(s) list. DO NOT list medications used to treat the AE. None

Concomitant Medication	Approximate Duration of Use
1.	
2.	
3.	
4.	
5.	
6.	

HPTN 035

Questions?