MTN-020
Data Communiqué #10

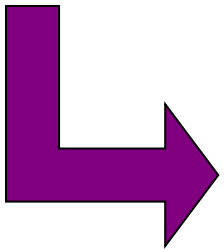
October 25, 2013

ASPIRE
A Study to Prevent Infection with a Ring for Extended Use

HIV and AE Reporting

- HIV acquisition (seroconversion) is not considered an AE for data collection or reporting purposes in ASPIRE as it is one of the study primary endpoints. Thus, “HIV Infection” *should not* be reported as an AE or written anywhere on an AE/GAE log CRF.

- However, as HIV acquisition is often symptomatic, a constellation of these accompanying symptoms may best be described as primary HIV infection illness.



Thus, if a participant seroconverts and develops one or more signs or symptoms of acute HIV-infection, it is appropriate to reports these sign(s)/symptom(s) as a single AE using **ONLY** the term “**seroconversion illness**” (Item 1 on AE/GAE-1 log CRF).

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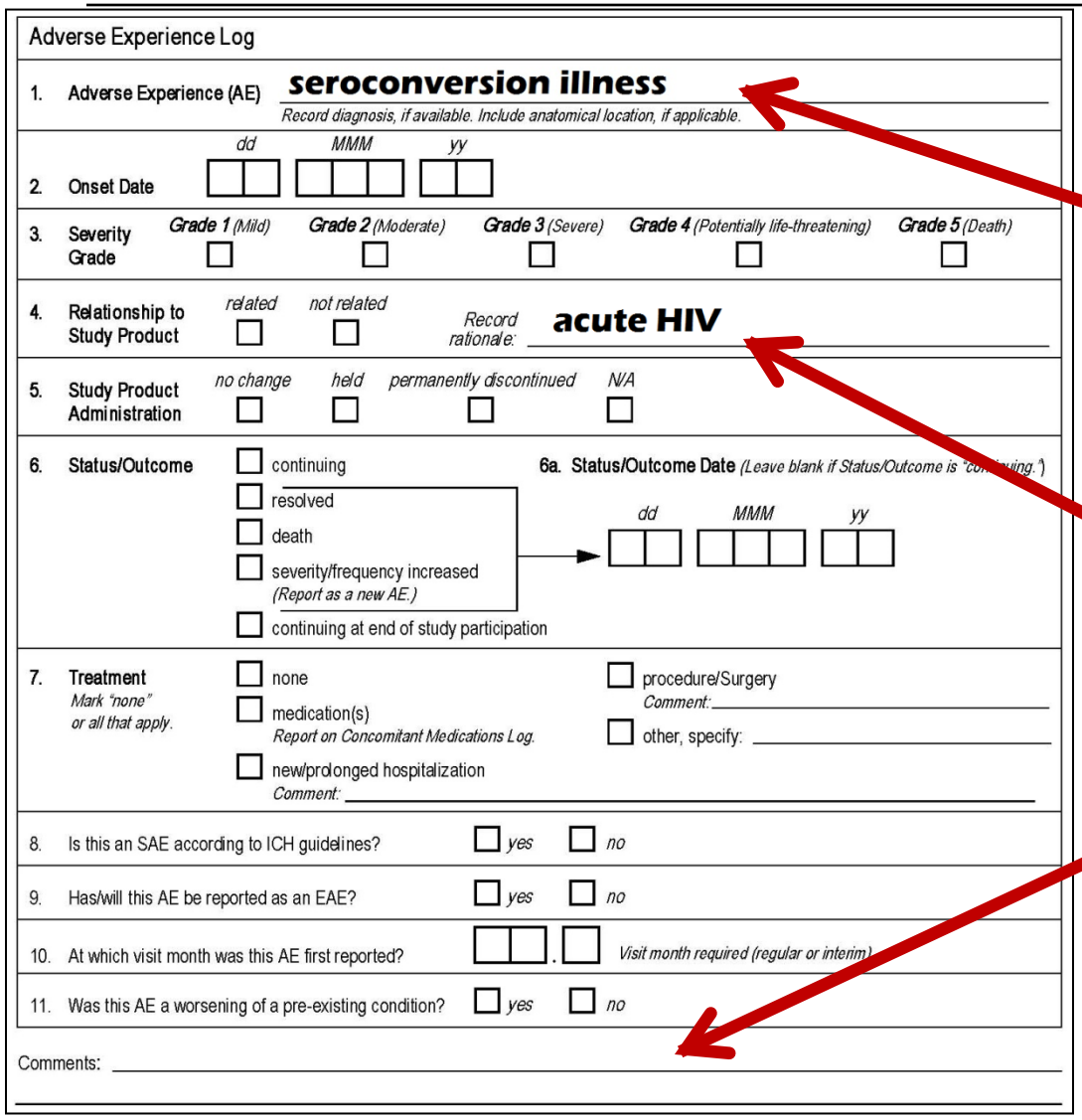
HIV and AE Reporting – AE/GAE Log CRF



Adverse Experience Log

1. Adverse Experience (AE): **seroconversion illness**
   Record diagnosis, if available. Include anatomical location, if applicable.
2. Onset Date: dd MMM yy
3. Severity Grade: Grade 1 (Mild) ☐ Grade 2 (Moderate) ☐ Grade 3 (Severe) ☐ Grade 4 (Potentially life-threatening) ☐ Grade 5 (Death) ☐
4. Relationship to Study Product: related ☐ not related ☐ Record rationale: **acute HIV**
5. Study Product Administration: no change ☐ held ☐ permanently discontinued ☐ N/A ☐
6. Status/Outcome: ☐ continuing; ☐ resolved; ☐ death; ☐ severity/frequency increased *(Report as a 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:* ____; ☐ procedure/Surgery *Comment:* ____; ☐ other, specify: ____
8. Is this an SAE according to ICH guidelines? ☐ yes ☐ no
9. Has/will this AE be reported as an EAE? ☐ yes ☐ no
10. At which visit month was this AE first reported? ☐☐.☐ *Visit month required (regular or interim)*
11. Was this AE a worsening of a pre-existing condition? ☐ yes ☐ no

Comments: ____

Report sign(s)/symptom(s) of acute HIV infection as a unifying diagnosis of "seroconversion illness" in Item 1.

On the rationale line for Item 4, record "acute HIV". To avoid a QC, ensure that the term 'acute' is always included.

Describe each HIV-related sign/symptom in the Comments Section.

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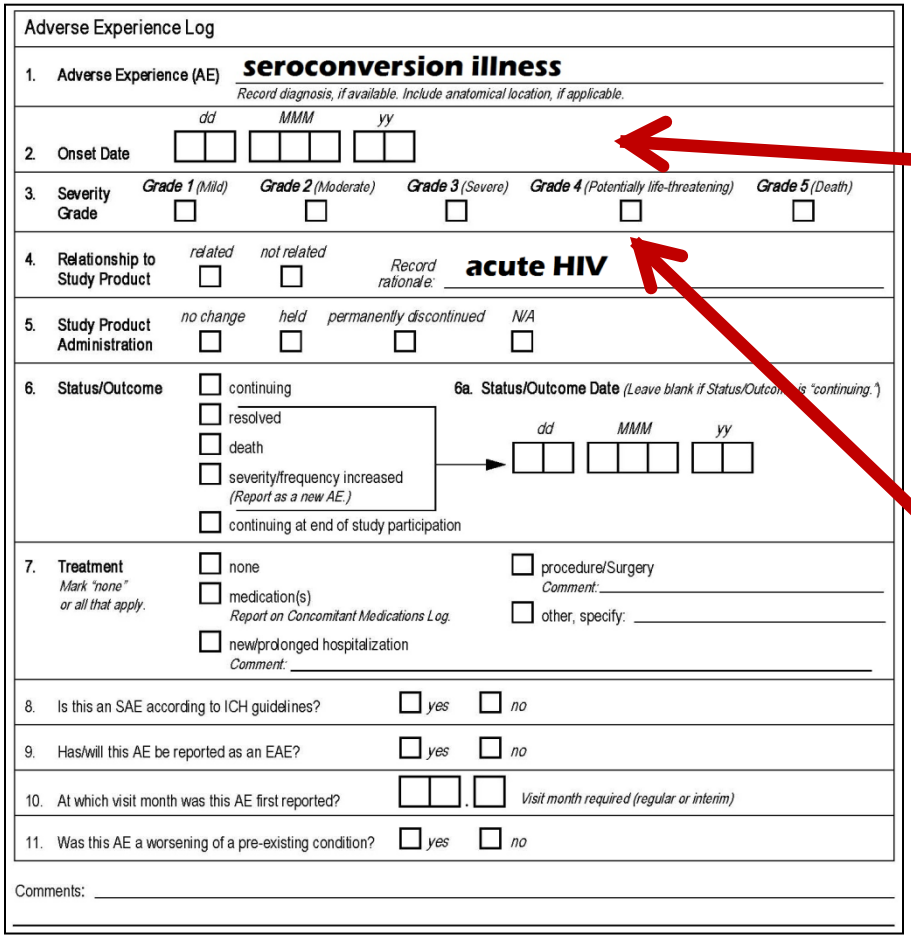
HIV and AE Reporting - AE/GAE Log CRF

- Complete other items on AE-1/GAE-1 log CRF per the general form instructions



Adverse Experience Log

1. Adverse Experience (AE) **seroconversion illness**
   Record diagnosis, if available. Include anatomical location, if applicable.
2. Onset Date — *dd* ☐☐ *MMM* ☐☐☐ *yy* ☐☐
3. Severity Grade — ☐ *Grade 1 (Mild)* ☐ *Grade 2 (Moderate)* ☐ *Grade 3 (Severe)* ☐ *Grade 4 (Potentially life-threatening)* ☐ *Grade 5 (Death)*
4. Relationship to Study Product — ☐ *related* ☐ *not related* *Record rationale:* **acute HIV**
5. Study Product Administration — ☐ *no change* ☐ *held* ☐ *permanently discontinued* ☐ *N/A*
6. Status/Outcome — ☐ continuing; ☐ resolved; ☐ death; ☐ severity/frequency increased *(Report as a 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:* ____; ☐ procedure/Surgery *Comment:* ____; ☐ other, specify: ____
8. Is this an SAE according to ICH guidelines? ☐ *yes* ☐ *no*
9. Has/will this AE be reported as an EAE? ☐ *yes* ☐ *no*
10. At which visit month was this AE first reported? ☐☐.☐ *Visit month required (regular or interim)*
11. Was this AE a worsening of a pre-existing condition? ☐ *yes* ☐ *no*

Comments: ____

"*Onset Date*" - date on which the participant first reported experiencing the first sign/symptom of acute HIV-infection

"*Severity Grade*" - if there is more than one sign/symptom, record the highest severity grade in item 3.

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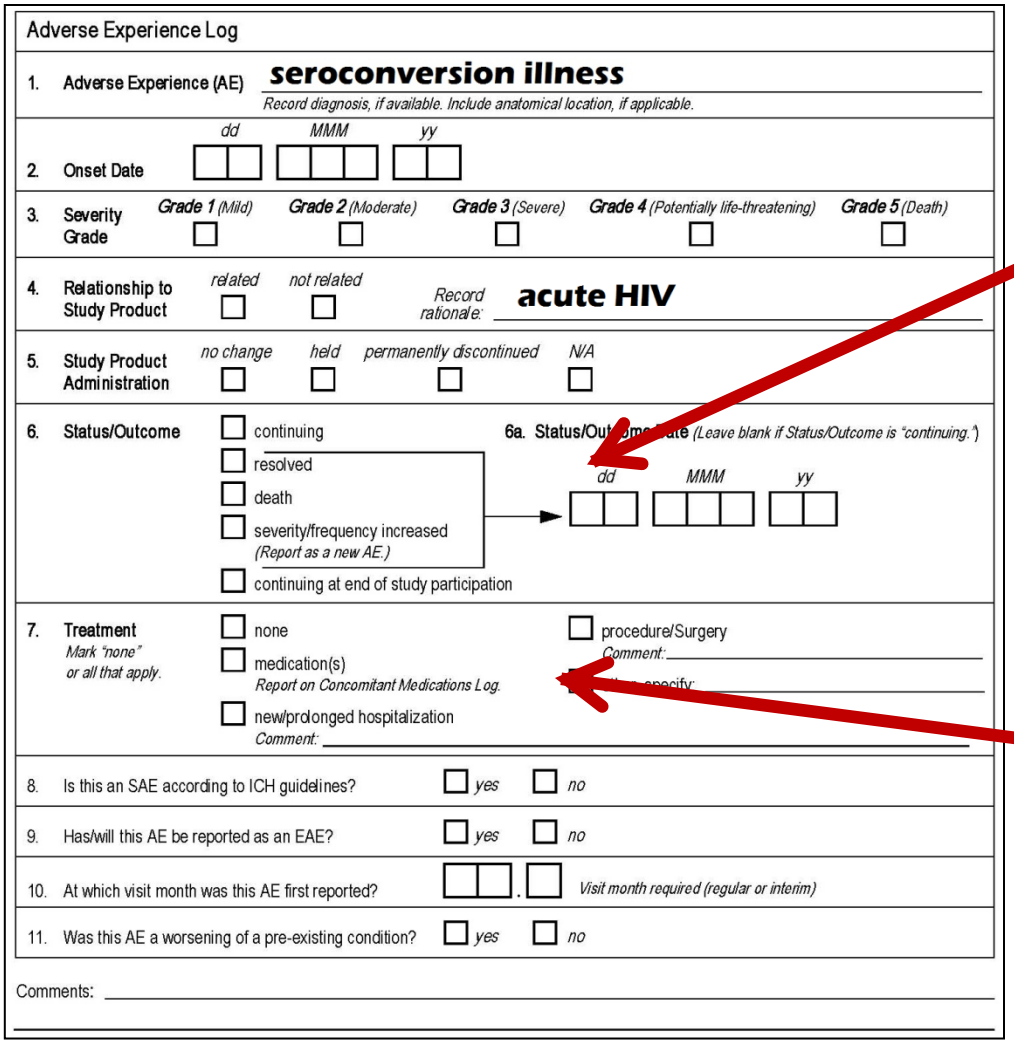
HIV and AE Reporting - AE/GAE Log CRF



Adverse Experience Log

1. Adverse Experience (AE): **seroconversion illness**
   Record diagnosis, if available. Include anatomical location, if applicable.
2. Onset Date: *dd* ☐☐ *MMM* ☐☐☐ *yy* ☐☐
3. Severity Grade: *Grade 1 (Mild)* ☐ *Grade 2 (Moderate)* ☐ *Grade 3 (Severe)* ☐ *Grade 4 (Potentially life-threatening)* ☐ *Grade 5 (Death)* ☐
4. Relationship to Study Product: *related* ☐ *not related* ☐ *Record rationale:* **acute HIV**
5. Study Product Administration: *no change* ☐ *held* ☐ *permanently discontinued* ☐ *N/A* ☐
6. Status/Outcome: ☐ continuing
   ☐ resolved
   ☐ death
   ☐ severity/frequency increased *(Report as a 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:* ____
   ☐ procedure/Surgery *Comment:* ____ *specify:* ____
8. Is this an SAE according to ICH guidelines? ☐ *yes* ☐ *no*
9. Has/will this AE be reported as an EAE? ☐ *yes* ☐ *no*
10. At which visit month was this AE first reported? ☐☐.☐ *Visit month required (regular or interim)*
11. Was this AE a worsening of a pre-existing condition? ☐ *yes* ☐ *no*

Comments: ____

"Status/Outcome" - AE resolved when all of the associated signs/symptoms have resolved or returned to baseline and any medications taken for the symptoms are no longer indicated.

"Treatment" – In item 7, mark any medications indicated and taken for the associated symptoms, if applicable, and report on CM-1.

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HIV and AE Reporting - AE/GAE Log CRF

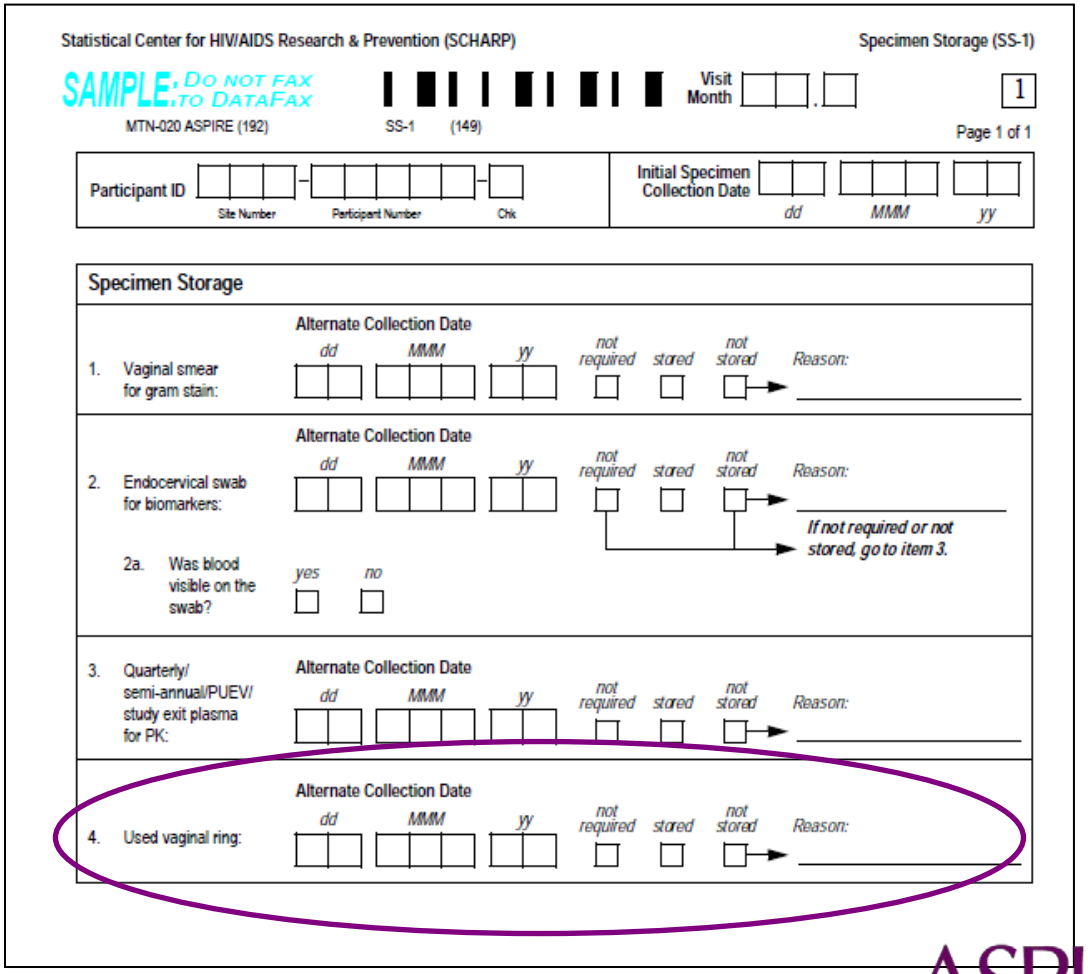
- If one or more signs/symptoms that have been reported on separate AE/GAE Log CRFs are later attributed to acute HIV-infection, change the earliest reported sign/symptom log page to the ‘seroconversion illness’ unifying diagnosis and list any other signs/symptoms in the comments section of this AE/GAE Log page.

- Mark any AE/GAE Log pages for the other signs/symptoms for deletion and write at the top of the page “Delete due to diagnosis on AE Log page (insert page #).”

- This new reporting guidance is considered in effect for all new AEs reported after the date of Data Communiqué #10. It is not necessary to review or modify previously reported AEs to comply with this new guidance.

Specimen Storage (SS-1) CRF now required at Monthly Visits

- Item 4 should be marked ‘stored’ at each scheduled monthly visit for all participants on study product
- For participants on temporary product holds or who are permanently discontinued, mark ‘not required’ for this item.



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

Specimen Storage (SS-1)

SAMPLE, DO NOT FAX TO DATAFAX

Visit Month ___.__ 1

MTN-020 ASPIRE (192) SS-1 (149)

Page 1 of 1

Participant ID ___-_____-___ (Site Number – Participant Number – Chk)

Initial Specimen Collection Date dd MMM yy

Specimen Storage

	Alternate Collection Date (dd / MMM / yy)	not required	stored	not stored	Reason:
1. Vaginal smear for gram stain:					
2. Endocervical swab for biomarkers:					
2a. Was blood visible on the swab?	yes / no				
3. Quarterly/ semi-annual/PUEV/ study exit plasma for PK:					
4. Used vaginal ring:					

If not required or not stored, go to item 3.

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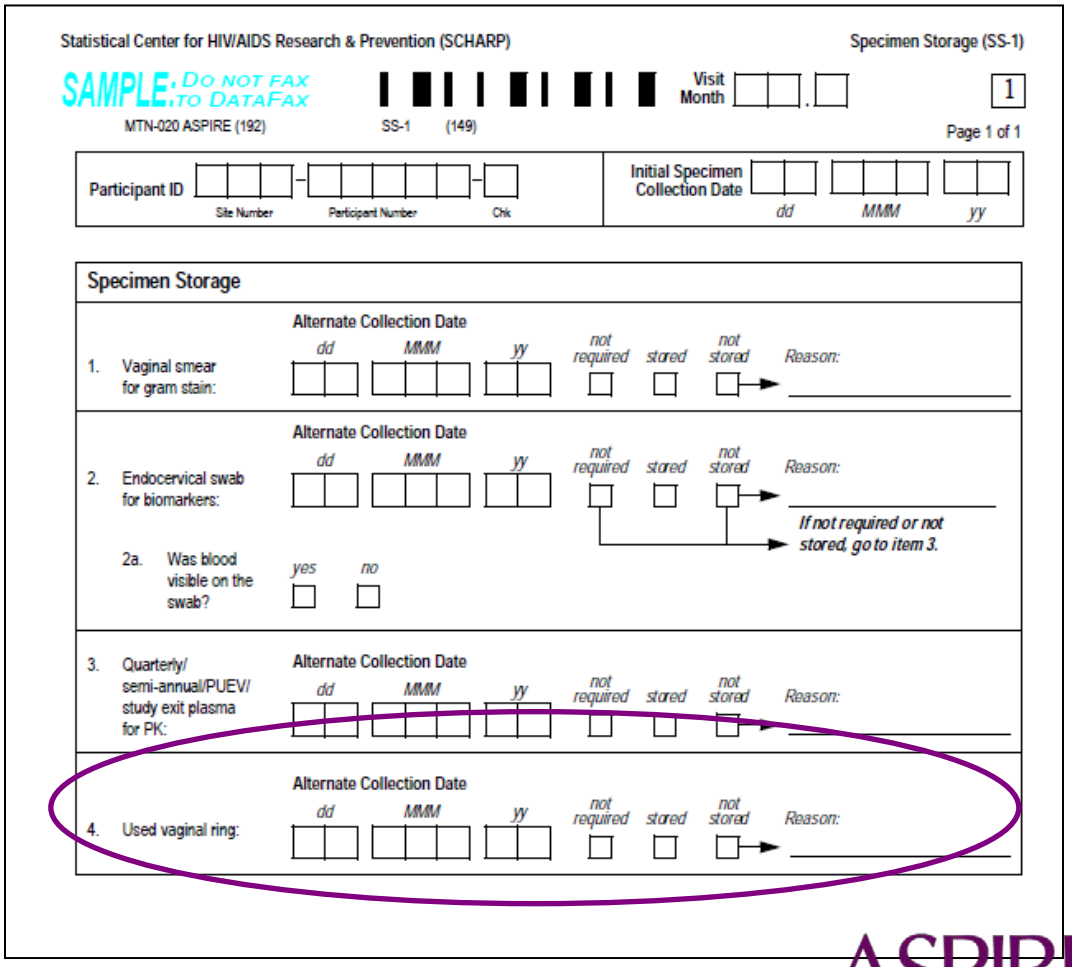
Specimen Storage (SS-1) CRF now required at Monthly Visits

- If the ring was required to be stored, but was not collected and/or stored, mark 'not stored' and provide the reason on the adjacent line.

- Possible reasons the ring was not stored include:
  - ✓ Participant lost the ring
  - ✓ Participant forgot to return ring
  - ✓ Participant declined ring at last visit
  - ✓ Ring was recently inserted at Interim Visit and she did not get a new ring at current visit
  - ✓ Any other reason ring was not available for storage


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

Specimen Storage (SS-1)

SAMPLE: DO NOT FAX TO DATAFAX

Visit Month

1

MTN-020 ASPIRE (192) SS-1 (149)

Page 1 of 1

Participant ID — Site Number — Participant Number — Chk

Initial Specimen Collection Date — dd MMM yy

Specimen Storage

	Alternate Collection Date (dd MMM yy)	not required	stored	not stored	Reason:
1. Vaginal smear for gram stain:					
2. Endocervical swab for biomarkers:					
2a. Was blood visible on the swab?	yes / no				
3. Quarterly/ semi-annual/PUEV/ study exit plasma for PK:					
4. Used vaginal ring:					

If not required or not stored, go to item 3.

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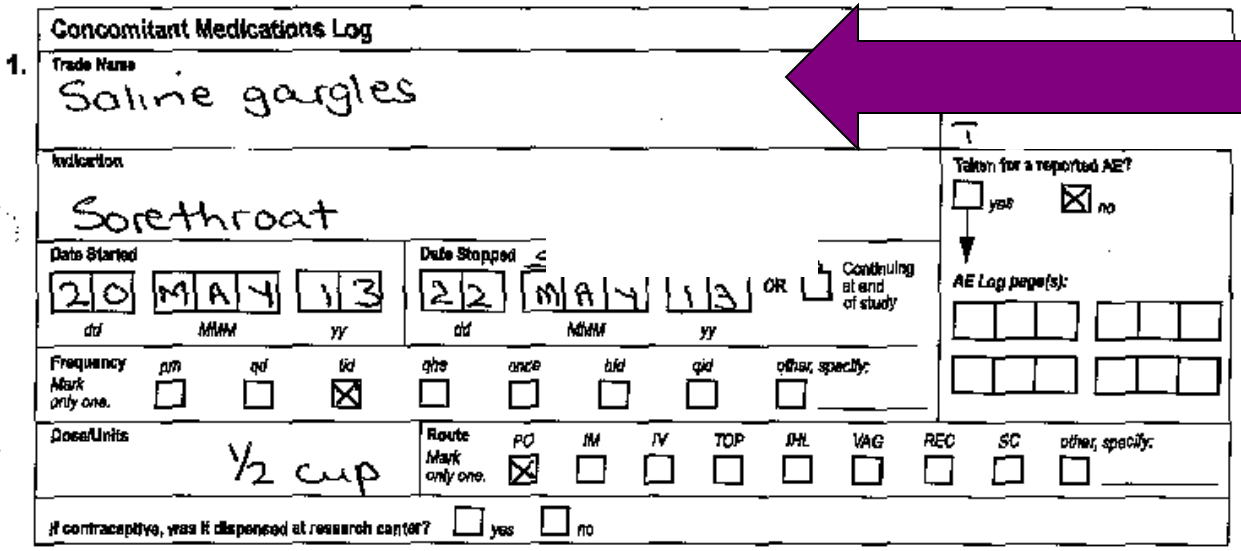
Concomitant Medications – Coding Queries

- Household products should not be reported as concomitant medications on the CM-1 Log CRF.
  - Examples include cleaners/solvents/Coca-Cola used for at-home douching, saline sitz baths, or saline gargles.



Concomitant Medications Log

1. Trade Name: Saline gargles

Indication: Sorethroat

Taken for a reported AE? ☐ yes ☒ no

AE Log page(s):

Date Started: 20 MAY 13 (dd MMM yy)

Date Stopped: 22 MAY 13 (dd MMM yy) OR ☐ Continuing at end of study

Frequency (Mark only one.): pm ☐ qd ☐ tid ☒ qhs ☐ once ☐ bid ☐ qid ☐ other, specify: ☐

Dose/Units: ½ cup

Route (Mark only one.): PO ☒ IM ☐ IV ☐ TOP ☐ INH ☐ VAG ☐ REC ☐ SC ☐ other, specify: ☐

If contraceptive, was it dispensed at research center? ☐ yes ☐ no

For example, saline gargles <u>do</u> <u>not</u> need to be reported on CM-1.

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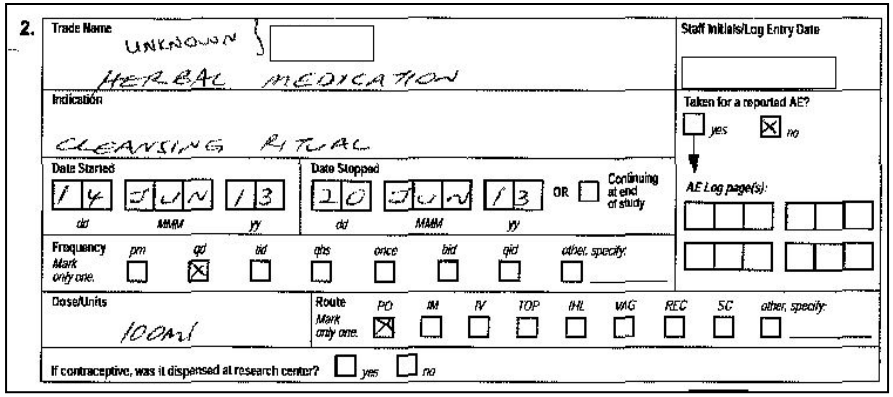
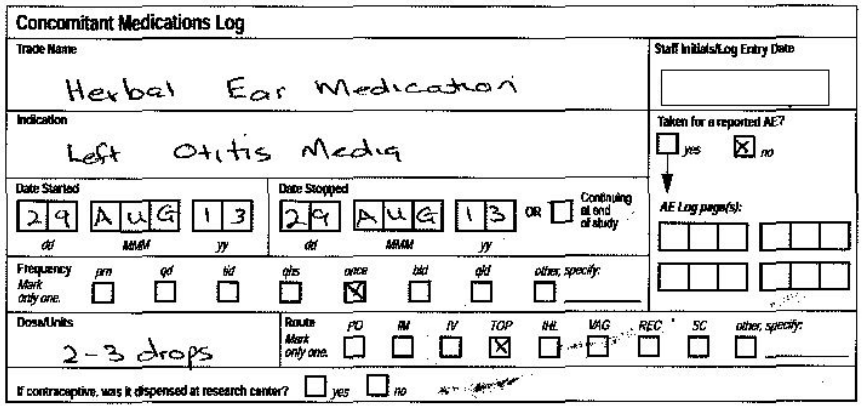
Concomitant Medications – Coding Queries

- Traditional herbal medicine should be reported as concomitant medications. If a medication includes more than one herb, list each herb separately on the CM-1 Log CRF.

Examples:


2.
Trade Name: UNKNOWN HERBAL MEDICATION
Staff Initials/Log Entry Date
Indication: CLEANSING RITUAL
Taken for a reported AE? yes no
Date Started: 14 JUN 13 (dd MMM yy)
Date Stopped: 20 JUN 13 (dd MMM yy) OR Continuing at end of study
AE Log page(s):
Frequency (Mark only one.): prn qd bid tid qhs once bid qid other, specify:
Dose/Units: 100ml
Route (Mark only one.): PO IM IV TOP IHL VAG REC SC other, specify:
If contraceptive, was it dispensed at research center? yes no


Concomitant Medications Log
Trade Name: Herbal Ear Medication
Staff Initials/Log Entry Date
Indication: Left Otitis Media
Taken for a reported AE? yes no
Date Started: 29 AUG 13 (dd MMM yy)
Date Stopped: 29 AUG 13 (dd MMM yy) OR Continuing at end of study
AE Log page(s):
Frequency (Mark only one.): prn qd bid tid qhs once bid qid other, specify:
Dose/Units: 2-3 drops
Route (Mark only one.): PO IM IV TOP IHL VAG REC SC other, specify:
If contraceptive, was it dispensed at research center? yes no

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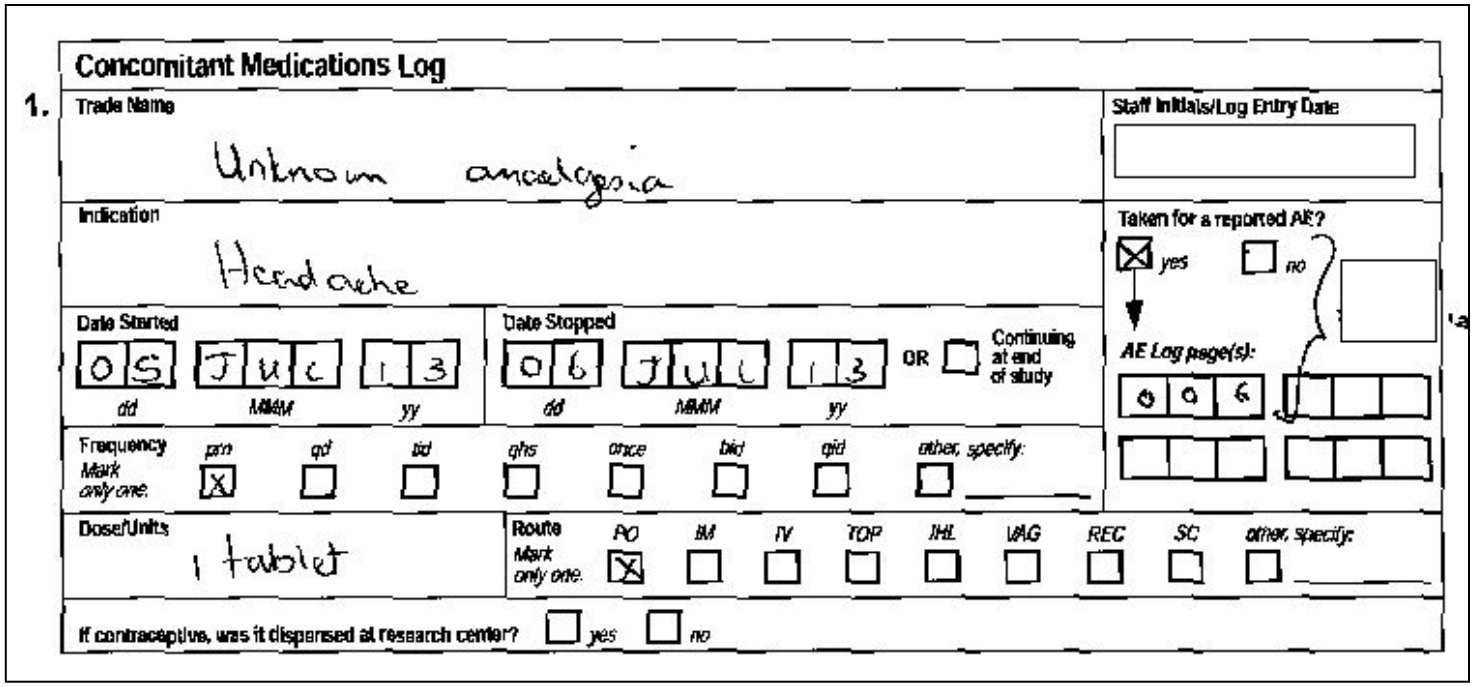
Concomitant Medications – Coding Queries

- If a medication's trade or generic name is unknown, record 'unknown', and a description or drug class.

For example:



Concomitant Medications Log

1. Trade Name: Unknown analgesic

Staff Initials/Log Entry Date:

Indication: Headache

Taken for a reported AE? [X] yes [ ] no

AE Log page(s): 006

Date Started: 05 JUL 13 (dd MMM yy)

Date Stopped: 06 JUL 13 (dd MMM yy) OR [ ] Continuing at end of study

Frequency (Mark only one): [X] prn [ ] qd [ ] bid [ ] qhs [ ] once [ ] bid [ ] qid [ ] other, specify:

Dose/Units: 1 tablet

Route (Mark only one): [X] PO [ ] IM [ ] IV [ ] TOP [ ] INH [ ] VAG [ ] REC [ ] SC [ ] other, specify:

If contraceptive, was it dispensed at research center? [ ] yes [ ] no

Questions?

- Please contact Jen Berthiaume and Karen Patterson with any questions you have about this slide presentation or the Data Communiqué.

Email us at:

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karenp@scharp.org

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