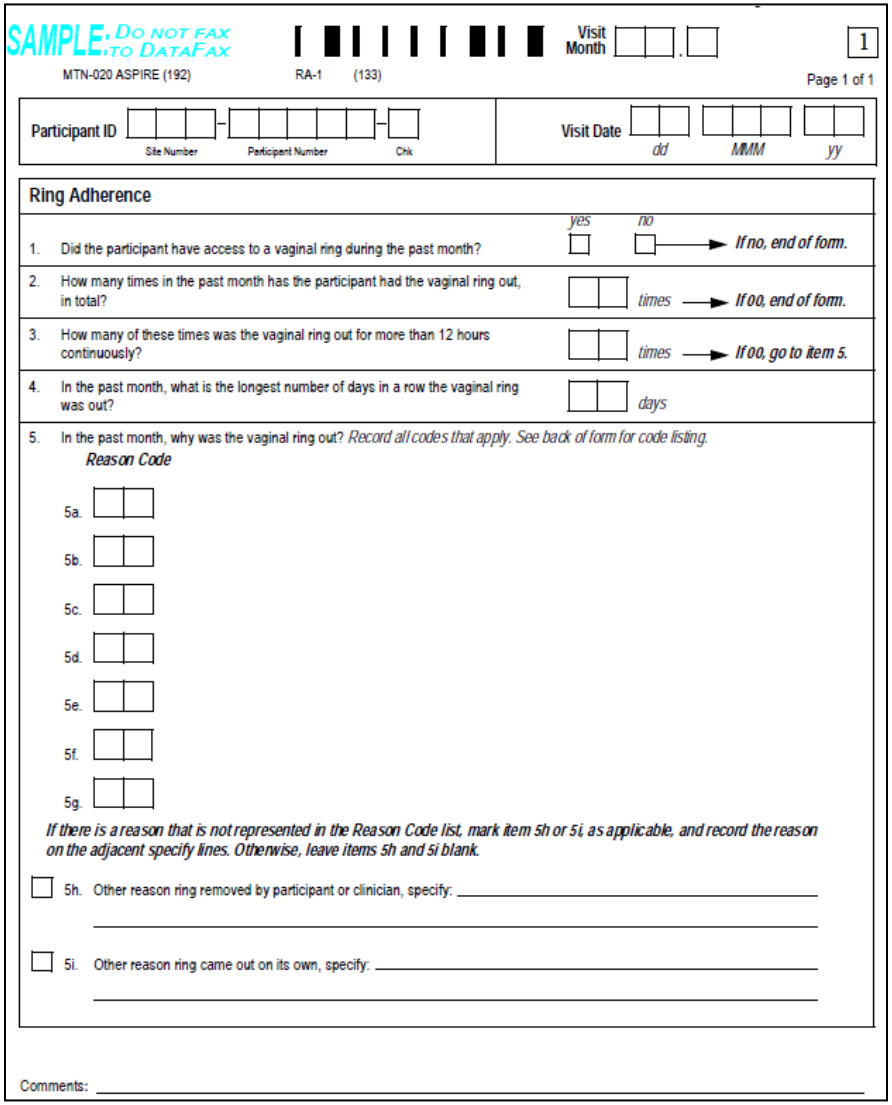
MTN-020
Data Communiqué #9

August 6, 2013

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

Updated Ring Adherence (RA-1) CRF Version 1.0 – 30Jul13



SAMPLE: DO NOT FAX TO DATAFAX

Visit Month ☐☐.☐ 1

MTN-020 ASPIRE (192) RA-1 (133) Page 1 of 1

Participant ID ☐☐☐-☐☐☐☐-☐ (Site Number – Participant Number – Chk)

Visit Date ☐☐ dd ☐☐☐ MMM ☐☐ yy

Ring Adherence

		yes	no	
1.	Did the participant have access to a vaginal ring during the past month?	☐	☐	→ *If no, end of form.*
2.	How many times in the past month has the participant had the vaginal ring out, in total?	☐☐ *times*		→ *If 00, end of form.*
3.	How many of these times was the vaginal ring out for more than 12 hours continuously?	☐☐ *times*		→ *If 00, go to item 5.*
4.	In the past month, what is the longest number of days in a row the vaginal ring was out?	☐☐ *days*		

5. In the past month, why was the vaginal ring out? *Record all codes that apply. See back of form for code listing.*

Reason Code

5a. ☐☐
5b. ☐☐
5c. ☐☐
5d. ☐☐
5e. ☐☐
5f. ☐☐
5g. ☐☐

If there is a reason that is not represented in the Reason Code list, mark item 5h or 5i, as applicable, and record the reason on the adjacent specify lines. Otherwise, leave items 5h and 5i blank.

☐ 5h. Other reason ring removed by participant or clinician, specify: _____

_____

☐ 5i. Other reason ring came out on its own, specify: _____

_____

Comments: _____

Form instructions:

- Item 4 text "in the past month" added to clarify that the longest number of days in a row the vaginal ring has been out applies to the past month only (maximum 31 days).
- The previous Item 5 response boxes have been replaced with Reason Code boxes.

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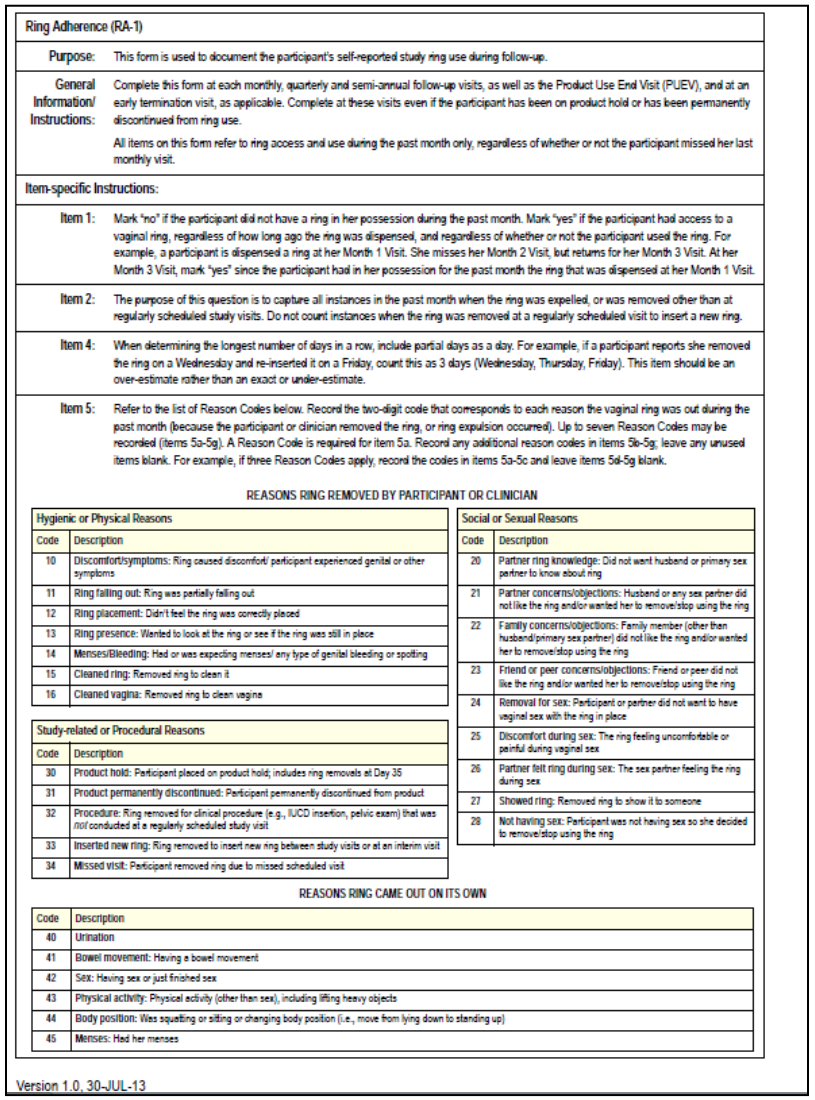
Updated Ring Adherence (RA-1) CRF Version 1.0 – 30Jul13



Ring Adherence (RA-1)

Purpose: This form is used to document the participant's self-reported study ring use during follow-up.

General Information/ Instructions: Complete this form at each monthly, quarterly and semi-annual follow-up visits, as well as the Product Use End Visit (PUEV), and at an early termination visit, as applicable. Complete at these visits even if the participant has been on product hold or has been permanently discontinued from ring use.

All items on this form refer to ring access and use during the past month only, regardless of whether or not the participant missed her last monthly visit.

Item-specific Instructions:

Item 1: Mark "no" if the participant did not have a ring in her possession during the past month. Mark "yes" if the participant had access to a vaginal ring, regardless of how long ago the ring was dispensed, and regardless of whether or not the participant used the ring. For example, a participant is dispensed a ring at her Month 1 Visit. She misses her Month 2 Visit, but returns for her Month 3 Visit. At her Month 3 Visit, mark "yes" since the participant had in her possession for the past month the ring that was dispensed at her Month 1 Visit.

Item 2: The purpose of this question is to capture all instances in the past month when the ring was expelled, or was removed other than at regularly scheduled study visits. Do not count instances when the ring was removed at a regularly scheduled visit to insert a new ring.

Item 4: When determining the longest number of days in a row, include partial days as a day. For example, if a participant reports she removed the ring on a Wednesday and re-inserted it on a Friday, count this as 3 days (Wednesday, Thursday, Friday). This item should be an over-estimate rather than an exact or under-estimate.

Item 5: Refer to the list of Reason Codes below. Record the two-digit code that corresponds to each reason the vaginal ring was out during the past month (because the participant or clinician removed the ring, or ring expulsion occurred). Up to seven Reason Codes may be recorded (items 5a-5g). A Reason Code is required for item 5a. Record any additional reason codes in items 5b-5g; leave any unused items blank. For example, if three Reason Codes apply, record the codes in items 5a-5c and leave items 5d-5g blank.

REASONS RING REMOVED BY PARTICIPANT OR CLINICIAN

Hygienic or Physical Reasons	
Code	Description
10	Discomfort/symptoms: Ring caused discomfort/ participant experienced genital or other symptoms
11	Ring falling out: Ring was partially falling out
12	Ring placement: Didn't feel the ring was correctly placed
13	Ring presence: Wanted to look at the ring or see if the ring was still in place
14	Menses/Bleeding: Had or was expecting menses/ any type of genital bleeding or spotting
15	Cleaned ring: Removed ring to clean it
16	Cleaned vagina: Removed ring to clean vagina

Social or Sexual Reasons	
Code	Description
20	Partner ring knowledge: Did not want husband or primary sex partner to know about ring
21	Partner concerns/objections: Husband or any sex partner did not like the ring and/or wanted her to remove/stop using the ring
22	Family concerns/objections: Family member (other than husband/primary sex partner) did not like the ring and/or wanted her to remove/stop using the ring
23	Friend or peer concerns/objections: Friend or peer did not like the ring and/or wanted her to remove/stop using the ring
24	Removal for sex: Participant or partner did not want to have vaginal sex with the ring in place
25	Discomfort during sex: The ring feeling uncomfortable or painful during vaginal sex
26	Partner felt ring during sex: The sex partner feeling the ring during sex
27	Showed ring: Removed ring to show it to someone
28	Not having sex: Participant was not having sex so she decided to remove/stop using the ring

Study-related or Procedural Reasons	
Code	Description
30	Product hold: Participant placed on product hold; includes ring removals at Day 35
31	Product permanently discontinued: Participant permanently discontinued from product
32	Procedure: Ring removed for clinical procedure (e.g., IUCD insertion, pelvic exam) that was not conducted at a regularly scheduled study visit
33	Inserted new ring: Ring removed to insert new ring between study visits or at an interim visit
34	Missed visit: Participant removed ring due to missed scheduled visit

REASONS RING CAME OUT ON ITS OWN

Code	Description
40	Urination
41	Bowel movement: Having a bowel movement
42	Sex: Having sex or just finished sex
43	Physical activity: Physical activity (other than sex), including lifting heavy objects
44	Body position: Was squatting or sitting or changing body position (i.e., move from lying down to standing up)
45	Menses: Had her menses

Version 1.0, 30-JUL-13

Form instructions:

- General information/Instructions, Items 1 & 2 updated to clarify intent of questions
- Reason Codes added to Item 5 instructions with bolded lead-in text for easy identification
- Reasons for ring removals grouped into new categories
- Reason codes 10 & 14 text amended per Data Communique #8
- Additional reasons added based on data review of site responses to date

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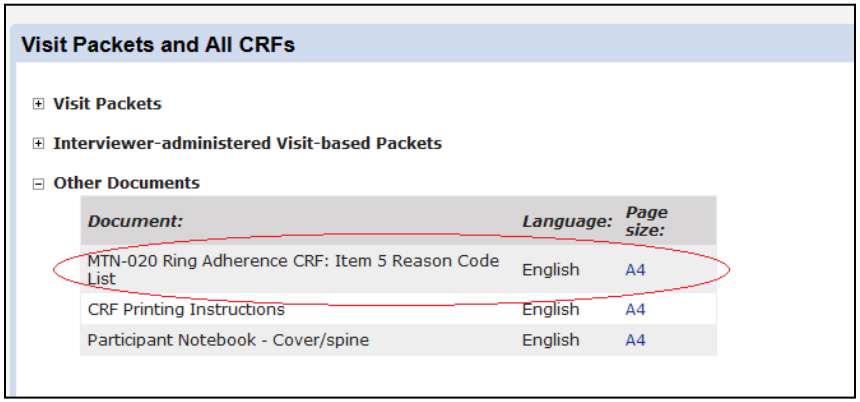
Updated Ring Adherence (RA-1) CRF Version 1.0 – 30Jul13

- Atlas Visit Packets have been updated to include new RA-1 CRF
- A separate document, “MTN020 Ring Adherence CRF: Item 5 Reason Code List” is available under ‘Other documents’ on Atlas as a reference to aid staff in completing item 5.



- Sites can begin transitioning to this new form immediately
- The previous RA-1 CRF may continue to be used until **August 12, 2013**. Starting on this date, all sites are expected to use the new version exclusively.

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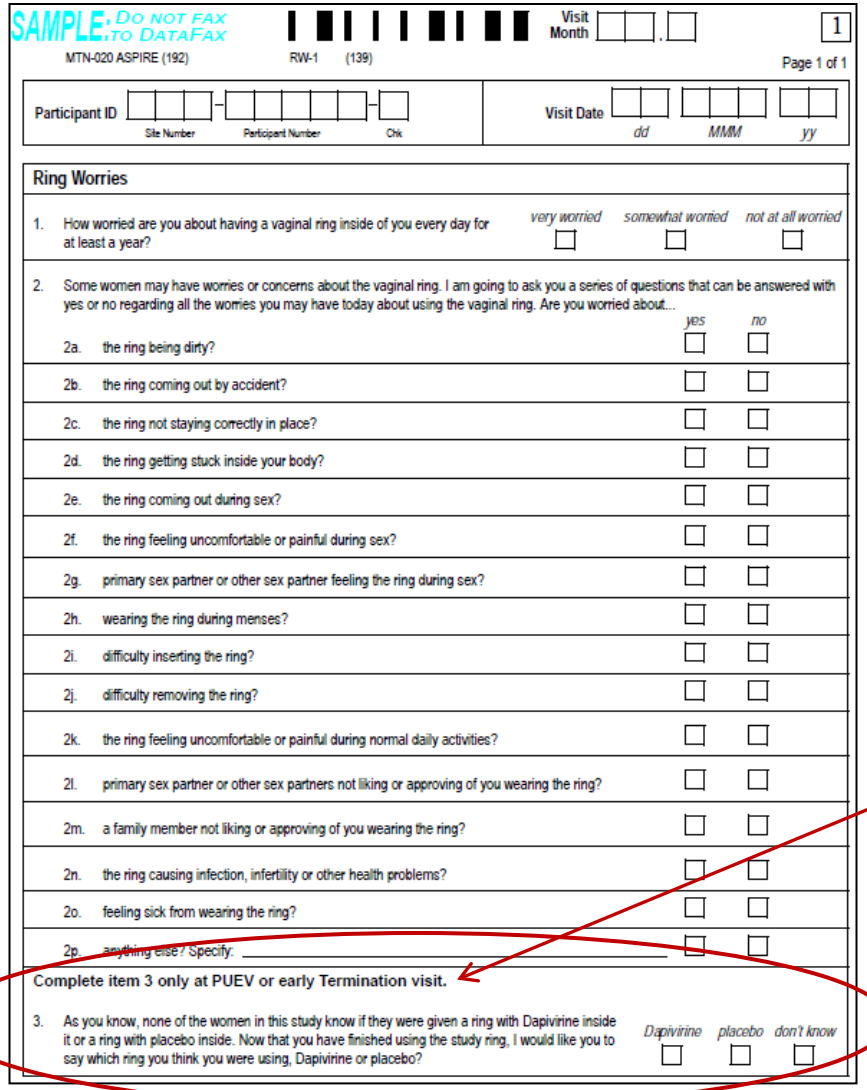
Ring Worries (RW-1), Item 3



SAMPLE: DO NOT FAX TO DATAFAX

Visit Month ☐☐.☐ 1

MTN-020 ASPIRE (192) RW-1 (139) Page 1 of 1

Participant ID ☐☐☐-☐☐☐☐-☐ (Site Number – Participant Number – Chk)

Visit Date ☐☐ dd ☐☐☐ MMM ☐☐ yy

Ring Worries

1.	How worried are you about having a vaginal ring inside of you every day for at least a year?	very worried ☐	somewhat worried ☐ / not at all worried ☐

2. Some women may have worries or concerns about the vaginal ring. I am going to ask you a series of questions that can be answered with yes or no regarding all the worries you may have today about using the vaginal ring. Are you worried about...

		yes	no
2a.	the ring being dirty?	☐	☐
2b.	the ring coming out by accident?	☐	☐
2c.	the ring not staying correctly in place?	☐	☐
2d.	the ring getting stuck inside your body?	☐	☐
2e.	the ring coming out during sex?	☐	☐
2f.	the ring feeling uncomfortable or painful during sex?	☐	☐
2g.	primary sex partner or other sex partner feeling the ring during sex?	☐	☐
2h.	wearing the ring during menses?	☐	☐
2i.	difficulty inserting the ring?	☐	☐
2j.	difficulty removing the ring?	☐	☐
2k.	the ring feeling uncomfortable or painful during normal daily activities?	☐	☐
2l.	primary sex partner or other sex partners not liking or approving of you wearing the ring?	☐	☐
2m.	a family member not liking or approving of you wearing the ring?	☐	☐
2n.	the ring causing infection, infertility or other health problems?	☐	☐
2o.	feeling sick from wearing the ring?	☐	☐
2p.	anything else? Specify: _____	☐	☐

Complete item 3 only at PUEV or early Termination visit.

3.	As you know, none of the women in this study know if they were given a ring with Dapivirine inside it or a ring with placebo inside. Now that you have finished using the study ring, I would like you to say which ring you think you were using, Dapivirine or placebo?	Dapivirine ☐	placebo ☐	don't know ☐

If a participant permanently discontinues from study product prior to her scheduled PUEV, complete <u>all items</u> on the RW-1 CRF, including Item 3, at the permanent discontinuation visit ***instead*** of the PUEV.

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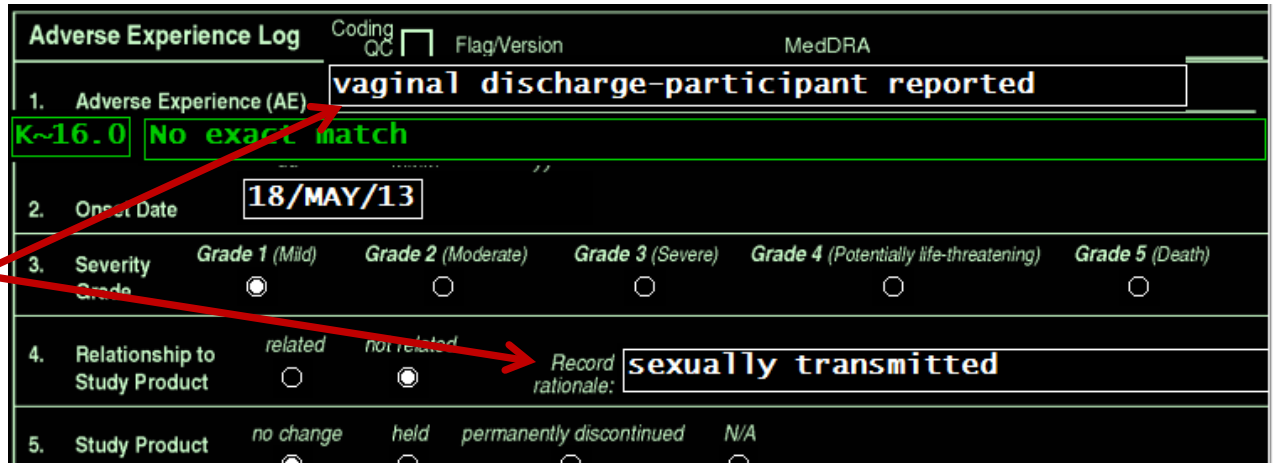
AE-1/GAE-1 Log CRFs – Item 4 Rationale

- If a previously completed GAE-1/AE-1 Log CRF page is updated with new information (for ex. a change to product relatedness or a medication taken for the AE), review other items on the page for consistency and update as needed.
  - If AE relationship to the vaginal ring changes due to test results confirming a diagnosis, **update both Item 1 and Item 4.**

Example 1:

To resolve CQC, AE Text (Item 1) should be updated to specify the STI to be consistent with the rationale in Item 4.

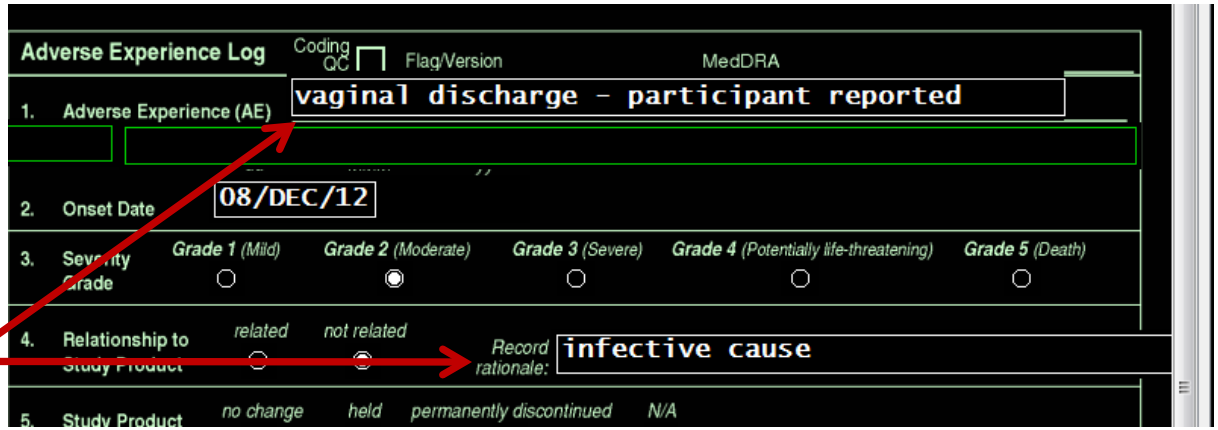


AE-1/GAE-1 Log CRFs – Item 4 Rationale

- If a previously completed GAE-1/AE-1 Log CRF page is updated with new information (for ex. A change to product relatedness or a medication taken for the AE), review other items on the page for consistency and update as needed.
  - If AE relationship to the vaginal ring changes due to test results confirming a diagnosis, **update both Item 1 and Item 4.**

Example 2:

To resolve CQC, AE Text (Item 1) should be updated to report 'vaginal infection' or 'vulvovaginitis' unless more specific dx is known
to be consistent with the rationale in Item 4.



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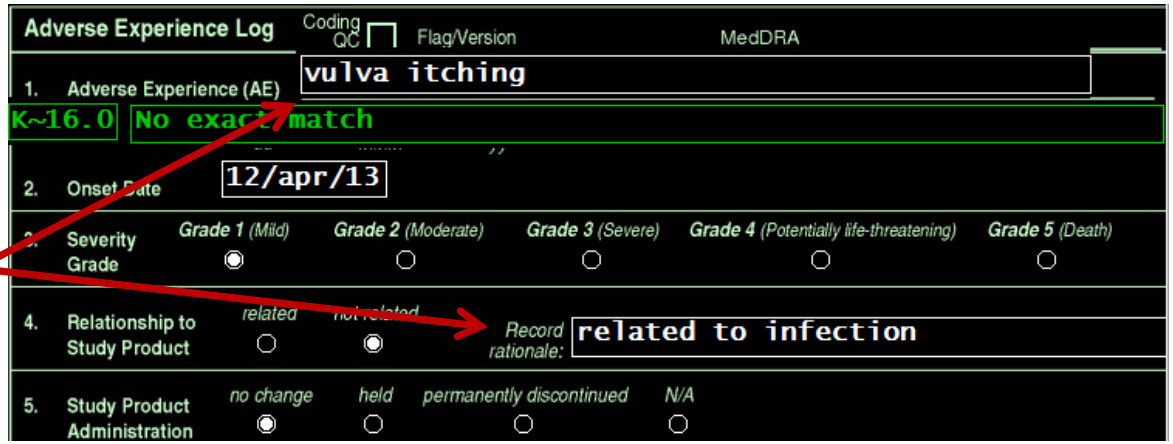
AE-1/GAE-1 Log CRFs – Item 4 Rationale

- If a previously completed GAE-1/AE-1 Log CRF page is updated with new information (for ex. A change to product relatedness or a medication taken for the AE), review other items on the page for consistency and update as needed.
  - If AE relationship to the vaginal ring changes due to test results confirming a diagnosis, **<u>update both Item 1 and Item 4.</u>**

Example 3:

To resolve CQC, AE Text (Item 1) should be updated to report "vulval infection' or 'vulvovaginitis' unless a more specific dx is known to be consistent with the rationale in Item 4.



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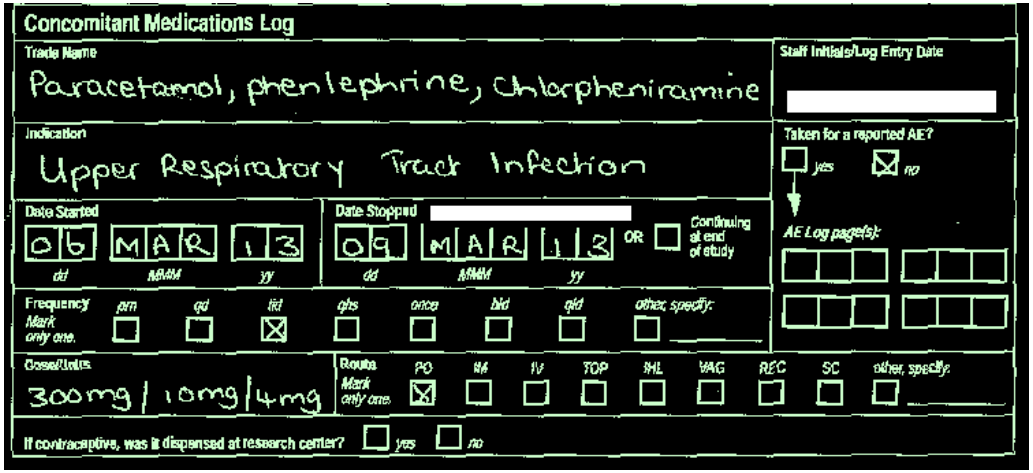
Concomitant Medications – Coding Query Examples

- If a trade name is not available/ or not reportable per national guidelines, record the generic name of the medication.

- A combination medication with a known generic name, can be recorded as one entry on the CM-1.

For example:



- If a combination medication does have a known generic name, ***each*** active ingredient must be reported as a <u>separate entry</u> in order to be accurately coded at SCHARP.

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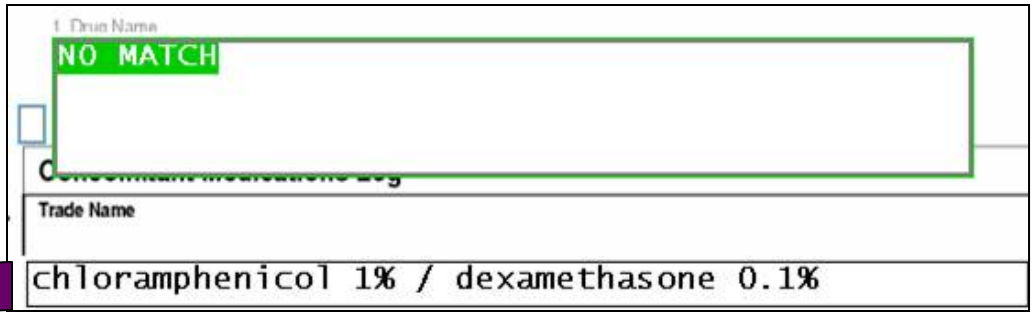
Concomitant Medications – Coding Query Examples

Example 1:

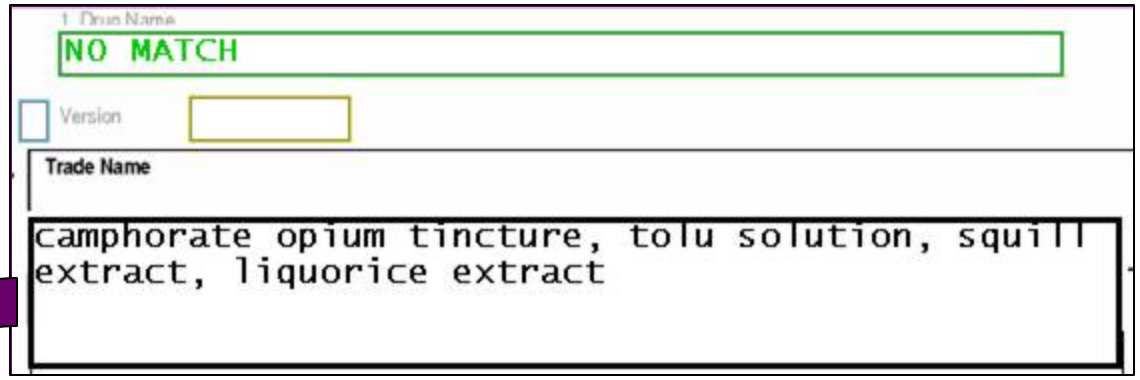


This item should be recorded as 2 separate entries on CM-1:

1. Chloramphenicol
2. Dexamethason

Concomitant Medications – Coding Query Examples

Example 2:



This item should be recorded as 4 separate entries on CM-1:

1. Camphorated tincture of opium
2. Tolu
3. Squill
4. Liquorice liquid extract

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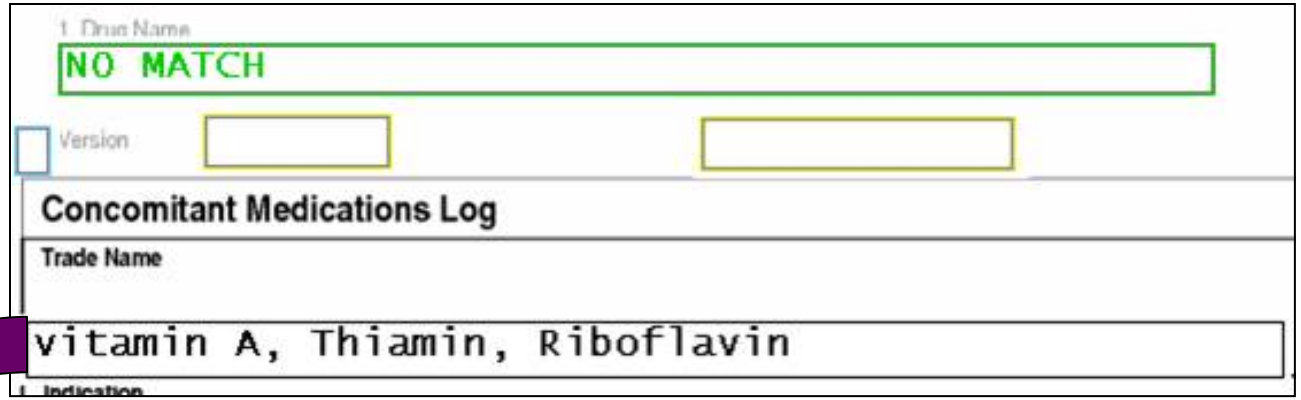
Concomitant Medications – Coding Query Examples

Example 3:



This item should be recorded as 3 separate entries on CM-1:

1. Vitamin A
2. Thiamin
3. Riboflavin

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Concomitant Medications – Coding Query Examples

- Minor spelling differences can affect the coding of medications. Please ensure the correct and consistent spelling of medications throughout the study.

Ex. 1: Aluminium Hydroxide vs. Aluminum Hydroxide

ALUMINIUM HYDROXIDE	00057401001
ALUMINIUM HYDROXID KENT PHARM	00057401024
ALUMINUM HYDROXIDE	00057401038
ALUMINIUM HYDROXID	00057401043

Ex. 2: Hydroxyzine vs. Hydroxizine

HYDROXYZINE	00058402009
HYDROXYZINUM	00058402015
NOVO-HYDROXYZIN	00058402018
HYDROXIZINE	00058402023

Ex. 3: Azithromycin Mylan vs. Azithromycine Mylan

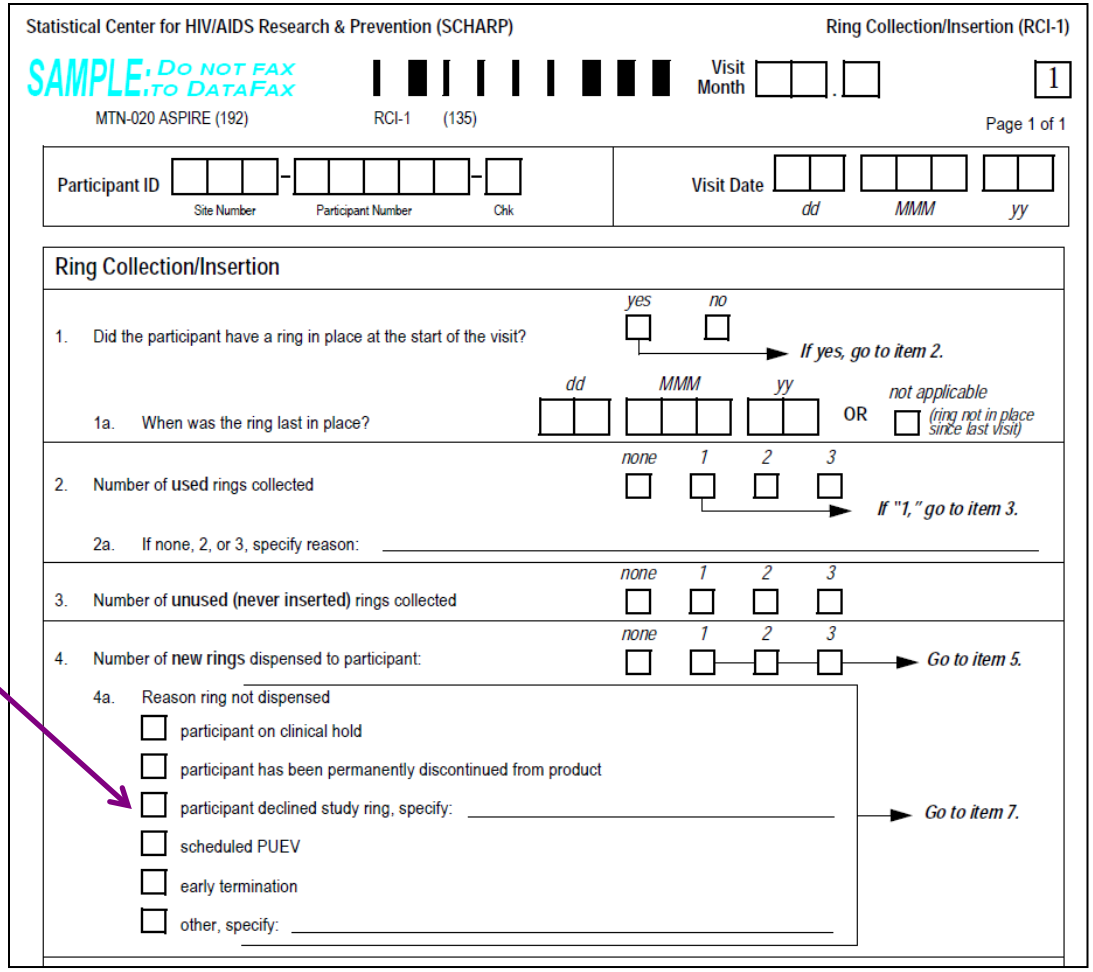
searchstring	drugcode
AZITHROMYCIN MYLAN	00944301450
AZITHROMYCINE MYLAN	00944304008

Ring Collection/Insertion (RCI-1) CRF – item 4a

Item 4a:

- If a new ring is not dispensed, mark 'participant declined the study ring' if the participant herself declined the study ring **OR** if the participant declined study ring due to family or partners' wishes.

- Provide details on the adjacent specify line.



Statistical Center for HIV/AIDS Research & Prevention (SCHARP) — Ring Collection/Insertion (RCI-1)

SAMPLE: DO NOT FAX TO DATAFAX

Visit Month ☐☐.☐ 1

MTN-020 ASPIRE (192) RCI-1 (135) Page 1 of 1

Participant ID ☐☐☐-☐☐☐☐-☐ (Site Number / Participant Number / Chk) Visit Date ☐☐ dd ☐☐☐ MMM ☐☐ yy

Ring Collection/Insertion

1. Did the participant have a ring in place at the start of the visit? ☐ yes ☐ no → *If yes, go to item 2.*

1a. When was the ring last in place? dd ☐☐ MMM ☐☐☐ yy ☐☐ OR ☐ not applicable (ring not in place since last visit)

2. Number of **used** rings collected ☐ none ☐ 1 ☐ 2 ☐ 3 → *If "1," go to item 3.*

2a. If none, 2, or 3, specify reason: _____

3. Number of **unused (never inserted)** rings collected ☐ none ☐ 1 ☐ 2 ☐ 3

4. Number of **new rings** dispensed to participant: ☐ none ☐ 1 ☐ 2 ☐ 3 → *Go to item 5.*

4a. Reason ring not dispensed

- ☐ participant on clinical hold
- ☐ participant has been permanently discontinued from product
- ☐ participant declined study ring, specify: _____ → *Go to item 7.*
- ☐ scheduled PUEV
- ☐ early termination
- ☐ other, specify: _____

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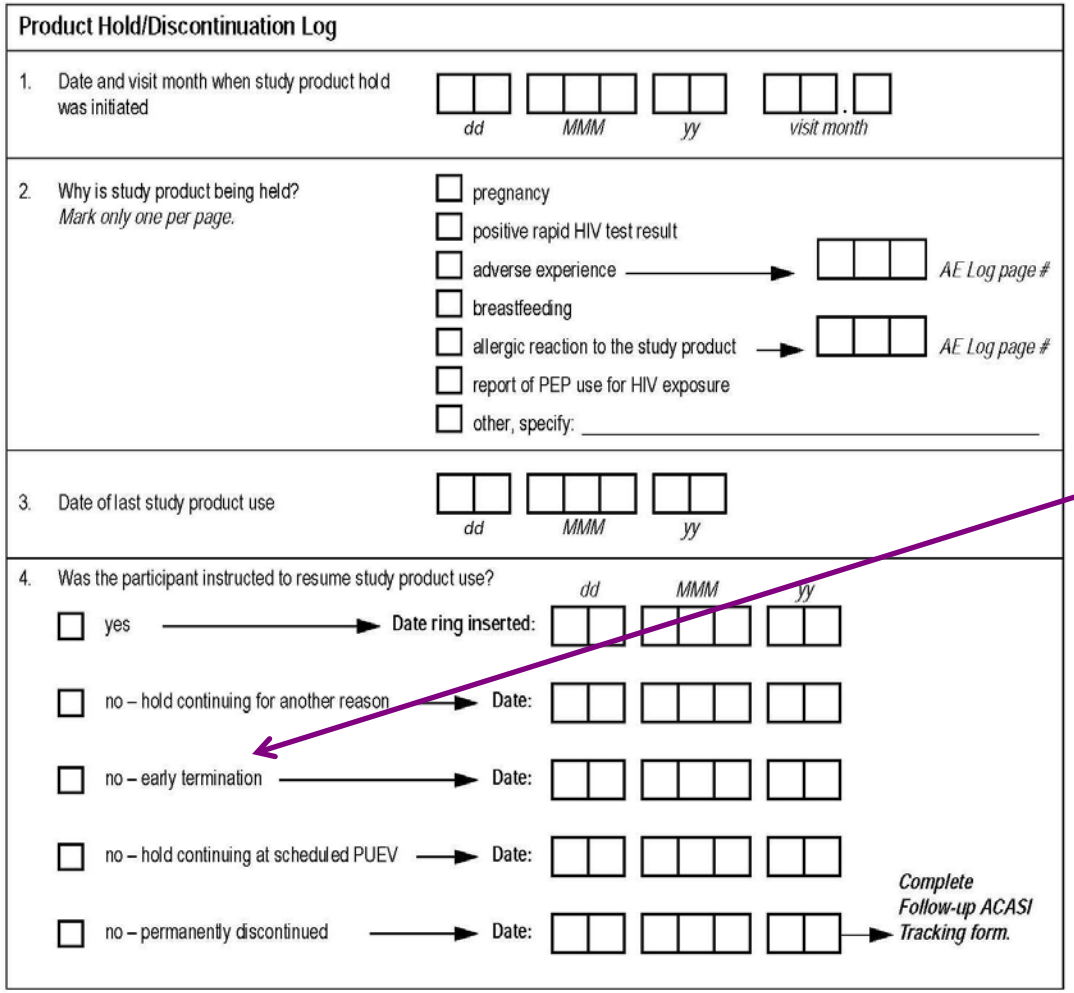
Product Hold/Discontinuation (PH-1) CRF – item 4



Product Hold/Discontinuation Log

1. Date and visit month when study product hold was initiated — dd / MMM / yy / visit month

2. Why is study product being held? *Mark only one per page.*
   - ☐ pregnancy
   - ☐ positive rapid HIV test result
   - ☐ adverse experience → AE Log page #
   - ☐ breastfeeding
   - ☐ allergic reaction to the study product → AE Log page #
   - ☐ report of PEP use for HIV exposure
   - ☐ other, specify: _____

3. Date of last study product use — dd / MMM / yy

4. Was the participant instructed to resume study product use? (dd / MMM / yy)
   - ☐ yes → Date ring inserted:
   - ☐ no – hold continuing for another reason → Date:
   - ☐ no – early termination → Date:
   - ☐ no – hold continuing at scheduled PUEV → Date:
   - ☐ no – permanently discontinued → Date: → *Complete Follow-up ACASI Tracking form.*

Item 4: "no - early termination" response

Mark "no-early termination" for Item 4 if a participant terminates early while the product hold is still in place and enter the date of the early termination visit.

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Questions?

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

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karenp@scharp.org

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