

## Section 14. Data Collection

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The purpose of this document is to provide site staff with the information they need to successfully complete and submit MTN-020 case report forms. For questions about this section or about general data collection policies, procedures, or materials, please contact the SCHARP Project Manager for the study as listed below.

The SDMC (Statistical and Data Management Center) for this study is SCHARP (the Statistical Center for HIV/AIDS Research and Prevention). SCHARP is located in Seattle, USA, and is in the US Pacific Time (PT) time zone. The SCHARP MTN-020 team members, along with their job role and e-mail address, are listed below.

### MTN-020 Statistical and Data Management Center (SDMC) Staff

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### 14.1 DataFax Overview

DataFax is the data management system used by SCHARP to receive and manage data collected at study sites. The site faxes an electronic image of each case report form (CRF) to SCHARP DataFax, and the original hard copy CRF is retained by the site.

#### CRF Transmission

Case report forms can be transmitted to SCHARP in one of two ways: faxed using a fax machine connected to a land phone line (fax to phone number 206.667.4805); or faxed using a fax machine connected to the internet (fax to e-mail <datafax@scharp.org>).

SCHARP's DataFax support group is available to consult with the site to determine the best method for data transmission. The DataFax support group can be contacted via e-mail at <support@scharp.org>. This group should also be contacted anytime the site has technical questions or problems with their fax equipment.

## Data Entry/Quality Control

Once a CRF image is received by SCHARP DataFax, the following occurs:

- DataFax identifies the study to which each CRF belongs using the barcode at the top of the form. It reads and enters the data into the study database and stores each CRF on a computer disk.
- Next, each CRF is reviewed by at least two members of SCHARP's Data Operations Group. Problems such as missing or potentially incorrect data are identified and marked with Quality Control notes (QCs).
- QCs are compiled into QC reports that are sent via e-mail to the study site on a regular basis. Sites are asked to correct or clarify any problems identified on the QC reports and refax the corrected CRFs to SCHARP DataFax.
- When the refaxed pages are received, SCHARP staff review the corrected pages and resolve the QCs.

If a change is made to a CRF but the updated page is not refaxed to SCHARP DataFax, the change will **not** be entered and the study database will continue to contain incomplete or incorrect data. Additionally, if the change was prompted by a QC, the QC will continue to appear on subsequent QC reports until the modified CRF is received at SCHARP. Therefore, it is very important that the site refax updated CRF pages to SCHARP DataFax **any time** a change is made to a CRF, regardless of whether or not the change was made in response to a QC report.

## 14.2 DataFax Form Completion

### 14.2.1 General Guidelines

Based on the use of fax technology and Good Clinical Practices (GCPs), the following guidelines should be used for completing DataFax CRFs:

- Use a black or dark blue medium ballpoint pen. Do not use any other type of writing tool. Use only one color per form. That is, do not begin completing a form using a blue pen and then switch to a black pen during the same form completion session.
- Press firmly when recording data or writing comments.
- Print all data and comments legibly by hand. Entries that cannot be read will result in QC notes.
- Do not type data onto CRFs. Do not use cursive/script handwriting, as it can be difficult to read.
- Write numbers as large as possible while staying within the boundaries of the boxes.
- Record data on the front of CRFs only. DataFax cannot read the back of CRFs.
- Do not record data or make marks in the 0.5-inch/1.5-cm margins at the top, bottom, or sides of the CRF.
- If the lines provided for written responses are not long enough, continue in another blank area of the form (within the page margins).
- Mark only one answer except when given the instruction "Mark all that apply."
- A response is required for every item unless instructed otherwise by a skip pattern.

- **Never** obscure, mark over, or punch holes through the barcode at the top of each CRF. DataFax requires the barcode to identify the CRF.
- **Never** use correction fluid (“white-out”) or correction tape on CRFs.
- Remove any paper clips, staples, or other attachments before faxing CRFs.
- The site staff person who initially completes the form **must** record his/her initials **and** the date in the space provided in the bottom right-hand corner of each CRF page.
- Fax forms as soon as possible after they have been completed and reviewed. Ideally, completed forms will be faxed to SCHARP within 1–2 days of completing the visit, though up to 5 days is allowed.

### 14.2.2 How to Mark Response Boxes

Many items on DataFax CRFs have a box or series of boxes for recording a response. Mark the box clearly with an **X**. Do not fill in the box with shading or mark it with a slash or other character.

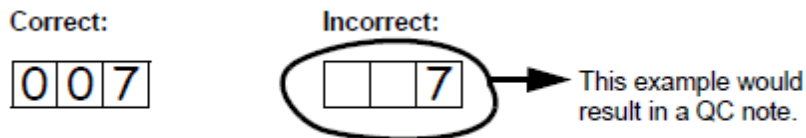


Mark only one response box for each item unless the “Mark all that apply” instruction is present.

### 14.2.3 How to Record Numbers

Some questions on DataFax CRFs include boxes for recording a numeric response. DataFax can only read the numbers in these boxes if they are recorded clearly. The following instructions should be followed when recording numeric responses:

- Right justify **all** numbers and fill in any blank leading boxes with zeroes. If boxes are left blank, a QC note will be applied asking for the boxes to be filled in.



The following example shows how a value of 7 is recorded when three response boxes are provided:

- Write the number(s) as large as possible while staying within the boundaries of the box; try not to stray outside the boundaries of the box.

In the following example, the 4 could be misinterpreted as a 7 or a 1 because DataFax can only read what is *inside* the box:

Correct:

4

Incorrect:

4

- Write the number(s) simply, with few loops.

The following example shows the format in which numbers will be most easily read by DataFax. Also included are some commonly used formats that may be difficult for DataFax to identify.

Easily Identified:

0 1 2 3 4 5 6 7 8 9

Difficult to Identify:

ø 1 2 3 4 7

#### 14.2.4 How to Record Dates

Dates are recorded using the “dd MMM yy” format, where “dd” represents the two-digit day, “MMM” represents the three-letter abbreviation of the month (in capital letters), and “yy” represents the last two digits of the year.

The month field must be filled in with the three-letter abbreviation *in English* for the date to be read in DataFax. Abbreviations are shown below:

Month	Abbreviation	Month	Abbreviation
January	<b>JAN</b>	July	<b>JUL</b>
February	<b>FEB</b>	August	<b>AUG</b>
March	<b>MAR</b>	September	<b>SEP</b>
April	<b>APR</b>	October	<b>OCT</b>
May	<b>MAY</b>	November	<b>NOV</b>
June	<b>JUN</b>	December	<b>DEC</b>

For example, June 6, 2012 is recorded as:

0	6	J	U	N	1	2
<i>dd</i>		<i>MMM</i>			<i>yy</i>	

Sometimes, only a month and a year are required (e.g., diagnosis date for a pre-existing condition), in which case the response boxes will look like this:

<i>MMM</i>			<i>yy</i>	

A diagnosis date of October, 2011 would be recorded as follows:

O	C	T	1	1
<i>MMM</i>			<i>yy</i>	

#### 14.2.5 How to Record Time

Time is recorded on DataFax CRFs using the 24-hour clock (00:00-23:59), in which hours are designated from 0–23. For example, in the 24-hour clock 2:25 p.m. translates to 14:25 (2 p.m. = 14), which would be recorded as follows:

1	4	:	2	5
<i>hr</i>			<i>min</i>	

Midnight is recorded as 00:00, not 24:00.

The following chart shows equivalencies between the 12- and 24-hour clocks:

12-hour clock (a.m.)	24-hour clock	12-hour clock (p.m.)	24-hour clock
Midnight	00:00	Noon	12:00

1:00 a.m.	01:00	1:00 p.m.	13:00
2:00 a.m.	02:00	2:00 p.m.	14:00
12-hour clock (a.m.)	24-hour clock	12-hour clock (p.m.)	24-hour clock
3:00 a.m.	03:00	3:00 p.m.	15:00
4:00 a.m.	04:00	4:00 p.m.	16:00
5:00 a.m.	05:00	5:00 p.m.	17:00
6:00 a.m.	06:00	6:00 p.m.	18:00
7:00 a.m.	07:00	7:00 p.m.	19:00
8:00 a.m.	08:00	8:00 p.m.	20:00
9:00 a.m.	09:00	9:00 p.m.	21:00
10:00 a.m.	10:00	10:00 p.m.	22:00
11:00 a.m.	11:00	11:00 p.m.	23:00

#### 14.2.6 Data Corrections and Additions

Sometimes, data on a DataFax CRF may need to be changed, clarified, or amended. There are many reasons why data may need to be changed, such as in response to a QC report or as a result of site review of the CRF before faxing.

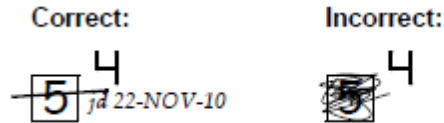
It is important to make these changes to the original CRF—**never** copy data onto a new form. After making the change, the CRF *must* be re-faxed to SCHARP DataFax.

**Note:** If a correction or addition is made to one page of a multiple-page CRF, only refax the page that was changed. Initial and date all changes or additions.

**Note:** Never write over an entry once it is recorded. Use the standards outlined in the following paragraphs when changing, clarifying, or amending data.

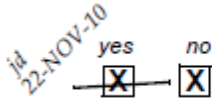
Whenever an entry on a DataFax CRF is changed, do the following:

- draw a single horizontal line through the incorrect entry (do not obscure the entry or make it un-readable with multiple cross-outs),
- place the correct or clarified answer near the box, and
- initial and date the correction as shown below:



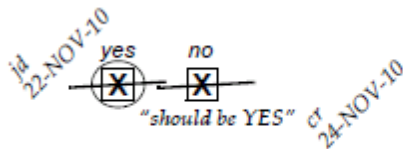
If an **X** is marked in the wrong response box, correct it by doing the following:

- draw a single horizontal line through the incorrectly marked box,
- mark the correct box, and
- initial and date the correction as shown below:



If the correct answer has previously been crossed out, do the following:

- circle the correct item,
- write an explanation in the white space near the item, and
- initial and date all corrections as shown below:

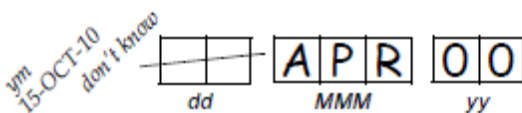


The standards above must **always** be followed whenever a CRF is changed, clarified, or amended, even if the change is made **before** the CRF is faxed to SCHARP for the first time.

#### 14.2.7 How to Handle Missing and Unknown Data

If the answer to an item is not known, is not available, or if the participant refuses to answer, draw a single horizontal line through the blank boxes and initial and date the item. It is helpful to write "don't know," "refuses to answer," "UNK" (unknown), "N/A" (not applicable), or "REF" (refused) near the blank boxes.

For example, when recording a date, if the exact day is not known, draw a single horizontal line through the "dd" boxes and write "don't know" next to the response boxes, as shown below:



A skip pattern is the **only** valid reason to leave a response blank. Initials and date are required for any data item that is refused, missing, unknown, or not applicable, regardless of whether it is marked as such during the initial form completion, or as an update to the form.

#### **14.2.8 Non-DataFax Forms**

Non-DataFax forms are case report forms that are used for data documentation purposes, but are not faxed to SCHARP. These forms are created to ensure consistent and accurate data documentation across study sites for data that is not needed in the study database. Non-DataFax form is easily identifiable because there is no DataFax barcode along the top of the CRF. In place of the barcode, the following text appears: "NOT A DATAFAX FORM. DO NOT FAX TO DATAFAX."

##### MTN-020 Grade 1 Adverse Experience Log

In addition to non-DataFax forms, there is one MTN-020 form with a barcode present, but that is not faxed to SCHARP. This is the Grade 1 Adverse Experience Log (GAE-1). This form is completed as instructed, but is not faxed to SCHARP. This form was created so that if the data are needed in the database, we can have the sites fax the form at that time. As of study start, we do not require these data in the database, so completed GAE-1 forms should not be faxed.

Both non-DataFax forms and the MTN-020 GAE-1 forms are completed using the general guidelines presented above, and completed forms are stored just as DataFax forms in participant files/binders.

#### **14.2.9 Faxing DataFax Forms**

Each CRF with a bar code at the top is a DataFax form, and is faxed to SCHARP DataFax once completed and reviewed as described in the site's MTN Data Management SOP. Sites are encouraged to develop a system that identifies each time a form page is faxed so that re-faxing of unchanged forms can be avoided. A date stamp used on the back of the form page may be used for this purpose as long as the date stamp does not obscure data recorded on the front of the form page.

For sites wishing to confirm the receipt by SCHARP of faxed forms, the CRF Tracking System (CTS) is available. This system generates two types of e-mails listings: 1) the number of form pages received at SCHARP for each batch of forms faxed; and 2) which specific individual form pages were received at SCHARP for a given PTID and visit. Please contact the SCHARP DataFax Support Group ([support@scharp.org](mailto:support@scharp.org)) if you would like to use the CRF Tracking System or for more information about this fax confirmation system.

#### **14.2.10 Form Storage**

Specifications for form storage are described in the site's MTN Data Management SOP. It is recommended that for each participant, study CRFs be stored in a hard-cover notebook, with a tabbed section for CRFs completed at each study visit.

It is suggested that log forms (such as the Concomitant Medications Log, Adverse Experience Log, Grade 1 Adverse Experience Log, Product Hold/Discontinuation Log, Protocol Deviations



Log, and Social Impact Log) be kept in their own tabbed sections within the participant study notebook. This makes page numbering and updating of these forms easier than if these forms are stored by visit within the participant's study notebook.

SCHARP can provide a template for use in creating notebook cover labels and spine labels. SCHARP can also provide a template that can be used to create tab divider labels.

#### 14.2.11 MTN Data Management SOP

As a condition for study activation, each study site must have an SOP for MTN Data Management. This SOP should be reviewed and followed in combination with the information contained in the study protocol, this SSP Manual, and the site's Clinical Quality Management Plan (CQMP).

The MTN Data Management SOP contains information on and outlines site staff responsibilities for several data topics, including:

- Participant ID (PTID) assignment
- Participant study file organization
- Participant confidentiality
- Site data quality control (QC) processes
- Timing of DataFax form data transmission
- SCHARP data QC processes
- Electronically-captured study data
- Data storage

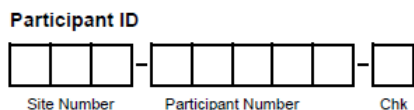
### 14.3 Study-Specific Data Collection Information

#### 14.3.1 Participant ID numbers (PTIDs)

DataFax uses a unique participant identification number (PTID) to identify each study participant in the database. Prior to study start, SCHARP provides each site with a list of PTIDs to be used for the study in the form of a study-specific MTN PTID Name-Linkage Log. The site assigns one PTID to each participant screened for the study. The PTIDs are assigned in sequential order as participants present for the screening visit. The site should ensure that each PTID is assigned only once. Once a participant has received a PTID, that same PTID is maintained for that participant for the duration of his/her study participation.

PTID boxes are located near the upper left corner of each CRF page.

The PTIDs used for this study are nine digits and formatted as "XXX-YYYYY-Z." The PTID consists of three parts: the DataFax site number (XXX), the participant number (YYYYY), and a numerical check digit (Z). The check digit (Z) is a number generated by SCHARP with the participant number, and helps ensure that the correct PTID is recorded. Below is an example of the PTID structure used in MTN-020.



### **14.3.2 Study Visit Timing**

#### **Screening and Enrollment**

The initial screening visit is defined as the day the participant provided written informed consent to be screened for the study. The enrollment visit will be scheduled to take place within 28 days of the initial screening visit. The date the participant is enrolled/randomized is Study Day 0 for the participant.

#### **Screening Attempts (Re-screens)**

If a participant's first screening attempt is unsuccessful, she may re-screen a maximum of one time for the study if she chooses. If she does re-screen, all screening procedures and forms must be repeated with the exception of PTID assignment and Eligibility Criteria CRF completion (see paragraph below). Once a PTID is assigned to a participant that PTID is used for the re-screen procedures and forms completed for that participant (do not assign a new PTID).

If a participant re-screens and enrolls in the study, only case report forms from the successful screening and enrollment visit are faxed to SCHARP. Note that in this case, the Eligibility Criteria CRF completed during the failed screening attempt should be updated and re-faxed with CRFs from the participant's successful screening and enrollment visits (do not complete a new Eligibility Criteria CRF for the successful screening attempt).

#### **Follow-Up Visits**

It is expected there may be up to 37 required follow-up visits for the MTN-020 study. For each of these visits, the visit type, visit code, target visit day, and visit window are listed in Table 14-1. Target days and windows are listed in days, with the day of enrollment/randomization as study day 0.

#### **Target Days and Visit Windows**

Whenever possible, visits should be completed on the target day. If not possible to complete the visit on the target day, the visit should be completed within the visit window.

SCHARP will provide sites with a spreadsheet tool that may be used to generate individual participant follow-up visit calendars. The spreadsheet requires that the participant's Enrollment date be entered. Once the enrollment date is entered, the target day and visit window for each required follow-up visit will appear. The calendar can then be printed and added to the participant's study notebook.

#### **Split Visits**

Enrollment Visits may not be split. Refer to the Accrual section of this manual for more information regarding Enrollment Visit procedures and timing.

Whenever possible, all required follow-up visit evaluations should be completed on the same day. In those cases where this is not possible, the participant may come back and complete the remaining evaluations on another day, as long as that day is within the visit window. For example, a participant comes in on her Month 3 target day and completes most of the required evaluations. She comes back 7 days later and completes the remaining required procedures.

This is allowed, and is referred to as a “split” visit; as the participant completed all required visit evaluations on two separate days, both days being in the visit window.

Note that for split visits, only one Visit Summary CRF is completed, and all CRFs completed for the visit are assigned the same visit month/code. The “Visit Date” on the Visit Summary CRF is the date of the first part of the split visit. See Section 14.3.3 for more information on assigning visit codes to split visits.

**Table 14-1: Visit Timing Requirements**

<b>MTN-020 Visit Windows</b>				
All windows are in days; Enrollment date = Day 0; PUEV=Product Use End Visit				
<b>Visit</b>	<b>Visit Code</b>	<b>Target Day</b>	<b>Window Opens</b>	<b>Window Closes</b>
<b>Screening</b>	97.0		28 days prior to Enrollment	
<b>Enrollment</b>	98.0	0 (min of 2 days post-menses)		28 days after Screening Visit
<b>Month 1</b>	01.0	28	14	41
<b>Month 2</b>	02.0	56	42	69
<b>Month 3</b>	03.0	84	70	97
<b>Month 4</b>	04.0	112	98	125
<b>Month 5</b>	05.0	140	126	153
<b>Month 6</b>	06.0	168	154	181
<b>Month 7</b>	07.0	196	182	209
<b>Month 8</b>	08.0	224	210	237
<b>Month 9</b>	09.0	252	238	265
<b>Month 10</b>	10.0	280	266	293
<b>Month 11</b>	11.0	308	294	321
<b>Month 12</b>	12.0	336	322	349
<b>Month 13</b>	13.0	364	350	377
<b>Month 14</b>	14.0	392	378	405
<b>Month 15</b>	15.0	420	406	433
<b>Month 16</b>	16.0	448	434	461
<b>Month 17</b>	17.0	476	462	489
<b>Month 18</b>	18.0	504	490	517
<b>Month 19</b>	19.0	532	518	545
<b>Month 20</b>	20.0	560	546	573
<b>Month 21</b>	21.0	588	574	601
<b>Month 22</b>	22.0	616	602	629
<b>Month 23</b>	23.0	644	630	657
<b>Month 24</b>	24.0	672	658	685
<b>Month 25</b>	25.0	700	686	713
<b>Month 26</b>	26.0	728	714	741
<b>Month 27</b>	27.0	756	742	769
<b>Month 28</b>	28.0	784	770	797
<b>Month 29</b>	29.0	812	798	825
<b>Month 30</b>	30.0	840	826	853
<b>Month 31</b>	31.0	868	854	881
<b>Month 32</b>	32.0	896	882	909
<b>Month 33</b>	33.0	924	910	937
<b>Month 34</b>	34.0	952	938	965
<b>Month 35</b>	35.0	980	966	993
<b>Month 36</b>	36.0	1008	994	1021
<b>Month 37</b>	37.0	1036	1022	1049
Maximum PUEV will be Month 36				
Maximum scheduled termination/study exit will be Month 37				

### Missed Visits

In those cases where a participant is not able to complete any part of a required follow-up visit within the visit window, the visit is considered “missed”. For example, an enrolled participant does not report to the clinic for her first follow-up visit until 43 days after enrollment. Per table 14-1, the Month 1 visit has been missed. The missed visit is documented in the study database by completion of a Missed Visit CRF.

### Interim Visits

An interim visit occurs when there is contact with the participant, but required follow-up visit procedures are not done, either because the required follow-up visit has already been completed, or it is too early in the visit window to complete the required visit. For example, an interim visit may occur via a phone contact if the participant reports a new AE requiring reporting on an AE-1 or GAE-1 CRF, or the participant is instructed by study staff to hold or permanently discontinue study product use.

All interim visits/contacts with the participant should be documented in a chart note. Additionally, if the interim contact results in at least one newly-completed DataFax CRF, the interim visit is assigned an interim visit code (visit code ending in something other than “.0”). All phone contacts that meet interim visit criteria per paragraph above are also assigned interim visit codes. See section 14.3.3 for information on how to assign visit codes to interim visits.

Note that for MTN-020, there is no Interim Visit CRF. Instead, a Visit Summary CRF is completed for interim visits/contacts as needed. Item 5 of the Visit Summary CRF will document whether the visit is a required (regular) visit or an interim visit.

The following are some examples of interim visits:

1. A participant comes in 12 days before her scheduled Month 8 visit (scheduled for the target day). She says she is coming back for her scheduled Month 8 visit, but needs more condoms today.

*Why interim visit? It is too early to conduct the Month 8 visit, so this is an interim visit. No visit code assigned since only procedure was condom provision, possibly counseling.*

2. A participant completes all required evaluations for her Month 5 on the target day. She then returns to the clinic 5 days later to request a new ring.

*Why interim visit? The participant has already completed all Month 5 procedures, and it is too early (and not in the visit window) for Month 6. This is an interim visit, conducted between Months 5 and 6, and is assigned an interim visit code as a new CRF will be completed (Visit Summary and Ring Collection/Insertion).*

3. A participant completes her Month 12 visit as scheduled. Her Month 13 visit window opens on July 12. The participant reports to the clinic unexpectedly on July 13 to report new genital AE symptoms.

*Why interim visit? The participant is in the Month 13 window, but it is too early to conduct the Month 13 visit. An interim visit code is assigned as new CRFs will be completed (Visit Summary, AE Log, possibly others).*

4. A participant completes all required evaluations for the Month 3 visit on the target day, May 15. Her labs do not come back until May 18, and she has a grade 4 ALT. The site contacts her by phone on May 18 and instructs her to remove the ring, as she is being placed on product hold due to the ALT result.

*Why interim visit? During the phone contact, the participant is being instructed by study staff to hold product use. An interim visit code is assigned, as a new Product Hold/Discontinuation Log and a new Adverse Experience Log will be completed as well as a Visit Summary CRF.*

5. A participant completes her Month 9 visit on the target day. The next day, she calls the clinic to report a new genital symptom.

*Why interim visit? During the phone contact, the participant reported a new symptom which will result in completion of a new CRF (AE Log). Since new CRFs are completed (AE Log and Visit Summary), an interim visit code is assigned.*

### 14.3.3 Visit Codes (Visit Months) and Page Numbers

Most CRFs will include boxes in the upper right corner for a “Visit Month” visit code. DataFax uses the visit code to identify the visit at which a CRF is completed. For CRFs completed only once per participant (the Enrollment CRF, for example), there is no place to record a visit code, as the visit code has been automatically assigned by SCHARP.

For MTN-020, note that none of the CRFs completed at the Screening or Enrollment visits has a place to record a visit code. SCHARP has automatically assigned visit codes to these two visits. The visit code assigned to the Screening Visit is 97.0, and for the Enrollment Visit, 98.0.

When “Visit Month” boxes are present, site staff is responsible for recording the appropriate visit month (code). For this study, the visit code recorded in the Visit Month boxes corresponds to the month of the visit. For example, for the Month 1 visit, record 01.0 for the Visit Month, for Month 2, record 02.0, for Month 13, record 13.0, and so on.

The table below lists the visit codes assigned to each required follow-up visit.

**Table 14-2: Visit Month/Visit Code Assignments for Required Follow-up Visits**

Visit Type	Visit Month/	Visit Type	Visit Month/ Visit	Visit Type	Visit Month/ Visit	Visit Type	Visit Month/ Visit
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	Visit Code		Code		Code		Code
Month 1	01.0	Month 11	11.0	Month 21	21.0	Month 31	31.0
Month 2	02.0	Month 12	12.0	Month 22	22.0	Month 32	32.0
Month 3	03.0	Month 13	13.0	Month 23	23.0	Month 33	33.0
Month 4	04.0	Month 14	14.0	Month 24	24.0	Month 34	34.0
Month 5	05.0	Month 15	15.0	Month 25	25.0	Month 35	35.0
Month 6	06.0	Month 16	16.0	Month 26	26.0	Month 36	36.0
Month 7	07.0	Month 17	17.0	Month 27	27.0	Month 37	37.0
Month 8	08.0	Month 18	18.0	Month 28	28.0		
Month 9	09.0	Month 19	19.0	Month 29	29.0		
Month 10	10.0	Month 20	20.0	Month 30	30.0		

### Visit Month/Codes for Split Visits

See Section 13.3.2 for a definition of split visits. When split visits occur, the CRFs completed for the visit are all assigned the same visit month, even though the dates will differ between some of the CRFs. For example, a participant comes in on her Month 6 target day of 23-AUG-12 and completes all required visit evaluations except the pelvic examination. She returns on 26-AUG-12 (still within the visit window) and completes the pelvic exam. All CRFs dated 23-AUG-12 and 26-AUG-12 are assigned the same Visit Month (visit code) of “06.0”.

### Visit Month/Codes for Interim Visits

Note that interim Visit Months/codes are not used for visits/contacts between the Screening Visit and Enrollment Visit, as CRFs completed for screening and enrollment have the visit month automatically-assigned.

For interim visits/contacts occurring between Enrollment and Month 1, assign interim visit months/codes starting with 98.1 (1<sup>st</sup> interim visit). Use a visit month/code of 98.2 for a 2<sup>nd</sup> interim visit between Enrollment and Month 1, 98.3 for the 3<sup>rd</sup> interim visit, etc.

For interim visits occurring after Month 1 onwards, interim Visit Months/codes are assigned using the following guidelines:

- In the two boxes to the left of the decimal point, record the two-digit visit month for the most recently required follow-up visit, *even if the visit was missed and/or if the participant is within the next visit's window.*
- For the box to the right of the decimal point:

- #.1 = the first interim visit after the most recently-required follow-up visit,
- #.2 = the second interim visit after the most recently-required follow-up visit,
- #.3 = the third interim visit after the most recently-required follow-up visit, and so on.

Example #1: A participant completes her Month 9 visit (Visit Month/code = 09.0) on the target day. She returns to the site one day later to report a new genital symptom. This interim Visit is assigned a Visit Month/code code of 09.1:

#### Visit Month/code for this Interim Visit

Visit Code 

0	9	.	1
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The examples below are from section 14.3.2, where interim visits are defined. These examples now have Visit Month/code information added to each example. :

1. A participant comes in 12 days before her scheduled Month 8 visit (scheduled for the target day). She says she is coming back for her scheduled Month 8 visit, but needs more condoms today.
 

*Why interim visit? It is too early to conduct the Month 8 visit, so this is an interim visit.*

**Visit Month/Code = not assigned (no new CRFs are completed for this visit – document in chart notes only).**
2. A participant completes all required evaluations for her Month 5 on the target day. She then returns to the clinic 5 days later to request a replacement ring.
 

*Why interim visit? The participant has already completed all Month 5 procedures, and it is too early for her to complete her Month 6 visit. This is an interim visit, conducted between Months 5 and 6.*

**Visit Month/code = 05.1.**
3. A participant completes her Month 12 visit as scheduled. Her Month 13 visit window opens on July 12. The participant reports to the clinic unexpectedly on July 13 to report new genital AE symptoms.
 

*Why interim visit? The participant is in the Month 13 window, but it is too early to conduct the Month 13 required visit.*

**Visit Month/code = 12.1.**
4. A participant completes all required evaluations for the Month 3 visit on the target day, May 15. Her labs do not come back until May 18, and she has a grade 4 ALT. The site contacts her by phone on May 18 and instructs her to remove the ring, as she is being placed on product hold due to the ALT result.
 

*Why interim visit? During the phone contact, the participant is being instructed by study staff to hold product use.*

**Visit Month/code = 03.1.**
5. A participant completes her Month 9 visit on the target day. The next day, she calls the clinic to report a new genital symptom.



*Why interim visit? During the phone contact, the participant reported a new symptom which will result in completion of a new DataFax CRF (the AE-1 Log CRF). This is an interim visit conducted between Months 9 and 10.*

**Visit Month/code = 09.1.**

### **Page Numbers**

Other CRFs, such as log forms (e.g., Adverse Experience Log or Concomitant Medications Log), may include boxes in the upper right corner for page numbers, as shown below:

Page 

--	--

Assign page numbers in sequential order, starting with 01 (or 001, for Adverse Experience Log CRFs). Assign numbers in sequential order (for example, the second Concomitant Medications Log page would be assigned page number 02, the third page would be assigned 03, and so on.

#### **14.3.4 Staff Initials/Date**

Most forms include a line in the lower-right corner for a staff member's initials and the date on which the form was completed. When more than one staff member records data on a CRF, the site should designate the staff member who has primary responsibility for the form. This individual completes the staff initials/date field. The individual not identified in the staff initials/date field writes his/her initials and date next to each data element for which he/she is responsible.

#### **14.3.5 Form Supply**

Sites are responsible for creating their own supplies of MTN-020 case report forms. Sites are encouraged to print CRFs from pdf files posted on the MTN-020 Atlas web page:

<https://atlas.scharp.org/cpas/project/MTN/020/begin.view?>

The pdf files provide CRFs by visit packets and also as individual forms. Each CRF visit packet will contain a cover page and all required non-translated CRFs required to be completed for the visit. Any local-language CRFs needed as well as any LDMS Sheets needed will be listed on the visit packet cover page, but not include in the packet file.

The individual CRF pdf files are used for CRFs use on an "as needed" basis, such as Adverse Experience Log forms.

#### **14.3.6 Case Report Form Completion Schedule**

The SCHARP-provided forms for this study include DataFax forms (forms that are completed and faxed to SCHARP DataFax) and non-DataFax forms (forms that are completed but not faxed to SCHARP DataFax).

Some SCHARP-provided forms are required to be completed at each visit, while other forms are required only at one visit or only when specifically indicated. The following table (Table 14-3) lists the DataFax and non-DataFax forms that are required to be completed at each study visit.

**Table 14.3: Schedule of Forms – CRFs Required to be Completed at Each Visit**

<p style="text-align: center;"><b>Screening Visit</b></p> <p>Demographics  Screening Pelvic Exam  Screening Visit Physical Exam  Screening Menstrual History  Screening Laboratory Results  Screening STI Test Results  Pre-existing Conditions  Concomitant Medications Log  Screening Specimen Storage  (non-DataFax) Pelvic Exam Diagrams  (non-DataFax) Screening Behavioral Eligibility  (non-DataFax) Screening Visit LDMS  Specimen Tracking Sheet</p> <p><b><i>If participant will not enroll:</i></b>  Eligibility Criteria</p>	<p style="text-align: center;"><b>Quarterly Visits (Months 3, 9, 15, 21)</b></p> <p>Visit Summary  Monthly Laboratory Results  Ring Adherence  Family Planning  Ring Collection/Insertion  Quarterly Laboratory Results  Behavior Assessment  Abbreviated Physical Exam  Specimen Storage  (non-DataFax) Follow-up LDMS Specimen  Tracking Sheet</p> <p><b>Additionally at Month 3:</b>  Ring Worries  Follow-up ACASI Tracking  Prevention Study Experiences</p>
<p style="text-align: center;"><b>Enrollment Visit</b></p> <p>Enrollment  Prior Trial Participation  Baseline Family Planning  Baseline Behavior Assessment  Baseline Vaginal Practices  Enrollment Abbreviated Physical Exam  Eligibility Criteria  (non-DataFax) Enrollment Behavioral Eligibility  (non-DataFax) Enrollment Visit LDMS  Specimen Tracking Sheet</p>	<p style="text-align: center;"><b>Semi-annual Visits (Months 6, 12, 18, 24)</b></p> <p>Visit Summary  Monthly Laboratory Results  Ring Adherence  Family Planning  Ring Collection/Insertion  Quarterly Laboratory Results  Behavior Assessment  Abbreviated Physical Exam  Specimen Storage  Pelvic Exam  Vaginal Practices  STI Test Results  (non-DataFax) Pelvic Exam Diagrams  (non-DataFax) Follow-up LDMS Specimen  Tracking Sheet</p> <p><b>Additionally at Month 12:</b>  Prevention Study Experiences</p>
<p style="text-align: center;"><b>Monthly Visits (Months 1, 2, 4, 5, 7, 8, etc.)</b></p> <p>Visit Summary  Monthly Laboratory Results  Ring Adherence  Family Planning  Ring Collection/Insertion  Specimen Storage  (non-DataFax) Follow-up LDMS Specimen  Tracking Sheet</p>	

<p style="text-align: center;"><b>PUEV (Product Use End Visit)</b> <i>Month will vary</i></p> <p>Visit Summary  Monthly Laboratory Results  Ring Adherence  Family Planning  Ring Collection/Insertion  Quarterly Laboratory Results  Behavior Assessment  Abbreviated Physical Exam  Specimen Storage  Pelvic Exam  Vaginal Practices  STI Test Results  PUEV Laboratory Results  Ring Worries  Follow-up ACASI Tracking  Social Influences Assessment  (non-DataFax) Pelvic Exam Diagrams n/a  (non-DataFax) Follow-up LDMS Specimen Tracking Sheet</p>	<p style="text-align: center;"><b>Early Termination</b> <i>Month will vary</i></p> <p>Visit Summary  Monthly Laboratory Results  Ring Adherence  Family Planning  Ring Collection/Insertion  Quarterly Laboratory Results  Behavior Assessment  Abbreviated Physical Exam  Specimen Storage  Pelvic Exam  Vaginal Practices  STI Test Results  PUEV Laboratory Results  Ring Worries  Follow-up ACASI Tracking  Termination TM-1  End of Study Inventory (non-DataFax) Pelvic Exam Diagrams n/a  (non-DataFax) Follow-up LDMS Specimen Tracking Sheet</p>
<p style="text-align: center;"><b>Scheduled Termination/Study Exit</b> <i>Month will vary</i></p> <p>Visit Summary  Specimen Storage  Monthly Laboratory Results  Study Exit Assessment  Termination TM-1  End of Study Inventory  (non-DataFax) Follow-up LDMS Specimen Tracking Sheet</p>	<p style="text-align: center;"><b>Interim Visits</b> <i>When a new CRF is completed</i></p> <p>Visit Summary  Other CRFS as needed</p>

#### 14.3.7 Completing Interviewer-administered Forms

In order to standardize interviewer-administered data collection from site to site and to maximize quality, it is critical that participant interviews be conducted with a non-biased, non-judgmental approach. Study staff should help a participant feel comfortable sharing personal information and opinions while asking the study questions in a consistent manner from participant to participant.

#### 14.3.8 Site Review (Quality Control) of DataFax Forms

As described in the site's MTN Data Management SOP (and referenced in the site's Clinical Quality Management Plan, CQMP), each site must perform two Quality Control (QC) review steps prior to faxing DataFax forms to SCHARP. While DataFax CRFs are being reviewed, it is important that they are stored and tracked systematically.

Below are specific review guidelines that should be followed for these QC review steps.

#### **14.3.8.1 MTN-020 QC Review Step #1**

- Review visit checklist and pelvic exam checklist (if used) to ensure all required procedures were completed
- Review CRFs based on participant responses to ensure completeness:
  - Screening Visit: Screening Behavioral Eligibility, Baseline Medical History Questions, Screening Menstrual History, Pelvic Exam Diagrams, Pre-existing Conditions, Concomitant Medications Log
  - Enrollment Visit: Enrollment Behavioral Eligibility, Eligibility Checklist, Baseline Family Planning, Baseline Behavior Assessment, Baseline Vaginal Practices, Enrollment Visit LDMS Specimen Tracking Sheet (non-DataFax), Prior Trial Participation, Pre-existing Conditions, Concomitant Medications Log
  - Follow-up visits, when present: Visit Summary (items 2 and 3), Ring Adherence, Behavior Assessment, Vaginal Practices, Ring Worries, Family Planning, Pelvic Exam Diagrams, Follow-up LDMS Specimen Tracking Sheet, AE/GAE Log CRFs

#### **14.3.8.2 MTN-020 QC Review Step #2**

This QC review step should occur before forms are faxed to SCHARP. Ideally, this review will happen once all lab results are available, so that all forms for a particular visit can be reviewed for consistency across documents. The goal, as outlined in the site's MTN Data Management SOP, is to correct data inconsistencies/errors prior to faxing forms to SCHARP so that QC notes are prevented.

General QC #2 procedures for all visits:

- Review visit checklist to ensure all required procedures were completed
- Ensure no participant identifies other than the PTID are present on DataFax forms.
- Ensure the PTID is correct, and is the same on all forms/documents.
- Ensure the Visit Month/Code assigned is correct, and is the same on all documents.
- Make sure a response has been recorded for each item, as required. Make sure skip patterns have been followed correctly.
- If a response box with "other", "specify", or "describe" line is present, ensure text is present on this line.
- Make sure text responses are clearly recorded.

Additional QC #2 procedures for Screening and Enrollment Visit documents:

- Review Screening Pelvic Exam, Screening Visit Physical Exam, Screening Laboratory Results, Screening STI Test Results, and Screening Menstrual History and ensure medical conditions are recorded appropriately on the Pre-existing Conditions form. Refer to the Pre-existing Conditions form instructions for further guidance.
- Ensure Screening Laboratory Results form has the correct Initial Specimen Collection Date. If any labs were repeated, complete a new form and use the Alternate Collection

Date as appropriate. If the participant enrolls, only fax the 2<sup>nd</sup> form completed to SCHARP.

- If a second (repeat) full pelvic exam is performed during screening, make sure a new Pelvic Exam Diagrams (non-DataFax) form is completed as well as a new Screening Pelvic Exam form is completed for the 2<sup>nd</sup> screening pelvic exam, and that only this form is faxed to SCHARP once the participant enrolls.
- Review Screening Specimen Storage form and make sure it matches information documented on the visit checklist and Screening Visit LDMS Specimen Tracking Sheet (or local lab requisition sheet).
- If participant will not enroll, make sure Eligibility Criteria form has been completed and faxed.
- Wait until the participant enrolls (is randomized) before faxing any CRFs to SCHARP. Once randomized and after Enrollment Visit CRFs have been reviewed, fax all Screening Visit and Enrollment Visit DataFax CRFs to SCHARP DataFax as appropriate.

Additional QC #2 procedures for follow-up visit documents:

- If AE Log is newly completed at a visit that is not an interim visit, make sure the Visit Summary CRF completed for the visit has item 6 marked “yes” (Visit Summary form with the same Visit Month as AE Log item 10).
- If Product Hold/Discontinuation Log is newly completed at a visit that is not an interim visit, make sure the Visit Summary CRF completed for the visit has item 7 marked “yes” (Visit Summary form with the same Visit Month as PH-1 item 1).
- On Family Planning form: if contraceptive marked requires documentation on Concomitant Medications Log (per instruction), make sure this is done accurately.
- Concomitant Medications Log: if “yes” marked for “Taken for a reported AE?”, make sure the AE Log page number recorded has “medication(s)” marked in item 7, and vice-versa. If the medication is a contraceptive, make sure there is a response marked for the “If contraceptive, was it dispensed at research center?” item.
- Follow-up ACASI Tracking: if item 1b is marked “scheduled PUEV” or “early termination”, make sure the Visit Summary form completed for the visit has matching information in item 4a.
- Visit Summary, item 5: if Item 5 is “yes”, ensure there is an interim Visit Month recorded on the form, and that items 6 and 7 are left blank.

#### 14.4 Form-Specific Completion Instructions

Detailed form completion instructions for each form are provided on the back of each form page. Some items on forms are straightforward and do not require specific instructions. Therefore, you will not see all form items listed in the form-specific completion instructions, but rather, only those items needing detailed explanation.

Below are additional instructions for some of the CRFs used in this study. These instructions do not appear on the back of the form page due to lack of space.

##### **Adverse Experience Log (AE-1)**

- Do not wait until the AE resolves before faxing the form page to SCHARP.

- Always make changes, corrections, and updates to the originally-completed form page (do not complete a new form). Once an AE Log form page has been started and faxed to SCHARP, the data from that page should never be transcribed onto another AE Log form page.
- Note that AE Log page numbers do not need to be assigned in any special order with regard to AE onset date or date reported to site. For example, if it is discovered that for a participant, page 001 and 003 were assigned, but not 002, simply assign page # 002 to the next AE Log form you complete. It does not matter if the AE's onset date or date reported to site on page 002 is later than these dates reported on AE Log page 003 (a QC will not be generated).
- For item 1, note that planned procedures or surgeries are not AEs. For example, a tonsillectomy is not an AE; rather, it is a treatment that will be collected in item 7. Any adverse experiences associated with the planned procedure or surgery, are AEs.

#### **Grade 1 Adverse Experience Log (GAE-1).**

- Always make changes, corrections, and updates are made to the originally-completed form page (do not complete a new form).
- Note that GAE Log page numbers do not need to be assigned in any special order with regard to AE onset date or date reported to site. For example, if it is discovered that for a participant, page 001 and 003 were assigned, but not 002, simply assign page # 002 to the next GAE Log form you complete. It does not matter if the AE's onset date or date reported to site on page 002 is later than these dates reported on AE Log page 003 (a QC will not be generated).

#### **14.4.1 CRF Completion Clarifications Contained in Data Communiques**

For ease of reference, the below is a listing of all CRF completion clarifications contained in Data Communiques #1 through #10.

##### **Data Communique #1**

###### Behavior Assessment, Item 15

If a participant reports a new social harm at a non-quarterly visit, mark Item 15 as 'yes' when next completed. For example, if a social harm is reported via a Social Impact Log CRF at Month 4, at Month 6 mark item 15 of the Behavior Assessment CRF as "yes". This way, the Month 6 Behavior Assessment CRF will accurately reflect that a new Social Impact Log has been completed since Month 3 (the most recent quarterly visit).

###### Concomitant Medications Log, Start Date form instruction for injectable medications

This instruction currently reads that when recording injectable medications, record each injection as a separate entry. This applies to contraceptive injectable medications only. Non-contraceptive injectables (like medications given in the hospital) may be recorded as a single entry.

###### Injection Contraceptive Medications injected prior to the Screening Visit

Injections of contraceptive medications used before the Screening Visit are not recorded on the Concomitant Medications Log CRF. This CRF only captures medications used on or after the Screening Visit date. If an injection used prior to the Screening Visit is recorded, this will result in a QC since the "Date Stopped" will be prior the Screening Visit date, and you will be asked to mark the

entry

Enrollment, Items 9-12 form instruction

The last sentence of this instruction (on the back of the CRF) currently reads “If any procedures are not completed, bring the participant back to the clinic for procedure completion as soon as possible.” We have since determined this sentence only applies to collection of plasma for archive. If plasma for archive was not collected on the day of randomization (Enrollment), the site should make every attempt to bring the participant back as soon as possible to collect and archive this specimen as part of an interim visit (prior to Month 1). Contact SCHARP with any CRF completion questions if this situation occurs.

Physical Exam CRFs (Screening, Enrollment, Abbreviated)

The CRF and database can only capture one blood pressure reading per visit. If more than one blood pressure reading is performed at a visit, record the blood pressure reading used for clinical assessment/management on the CRF. All other readings, along with a note explaining why multiple readings were taken, should be documented in the participant’s study file. Within the symptom-directed findings section of these CRFs, the “Notes” field is required for any item with “abnormal” marked. Sites may also record ‘Notes’ for items marked ‘normal’ (for example, if a normally –healed scar is noted as a normal finding).

Pre-Existing Conditions, severity grade

If a pre-existing condition is resolved as of the Enrollment Visit, do not make any changes to the severity grade (similar to what is done when resolving adverse events). Mark that the condition as not ongoing at Enrollment. If a pre-existing condition first identified at the Screening Visit, is ongoing at Enrollment, assess the severity at the Enrollment Visit and update the severity grade (up or down) as applicable to reflect the severity at the time of enrollment/randomization.

Protocol Deviations Log

Note that the actions documented in Items 7 and 8 (steps taken to address and prevent future deviations) are not required to be completed in order to transmit the CRF. The Protocol Deviation Log page should be transmitted to SCHARP once the CRF is completed, even if all of the actions/plans described in items 7 and 8 are still in-progress.

Screening Behavioral Eligibility item 17

This item asks the potential participant if she has participated in any other HIV prevention study using gel or tablet medications. Note that this question also includes HIV prevention studies that use a vaginal ring (IPM 027, for example) as well as HPTN 052. If a potential participant has been enrolled in IPM 027 or HPTN 052, she must wait until 12 months have passed since this study termination in order to be eligible for MTN-020. Note that MTN-001 participants are eligible based on this criterion, as the last termination visit for MTN-001 was July 30, 2010 (approximately 24 months prior to 020 initiation).

Screening Menstrual History, item 2 “specify” line for amenorrheic for past 6 months

If “amenorrheic for past 6 months” is marked, record on the “specify” line a brief description of why the participant is currently amenorrheic. For example, record on the specify line “Depo”, “contraception”, or “unknown”. More details can be provided in item 8 of the CRF as needed.

Screening Menstrual History, Items 3-7

Complete these items based on the participant’s usual menstrual periods as experienced prior to the Screening Visit. If the participant has been amenorrheic (consistently or partially), complete the items based on the description of her most recently-experience menstrual periods and provide additional details (as needed) in item 8. If the participant reports more than 99 days between her

usual menses, record “99” for item 3 (maximum boxes) and provide more details in item 8.

#### Screening STI Test Results, item 1b form instruction

This form instruction, which states that vaginal fluid pH is required at all semi-annual visits and the PUEV, while correct, it does not apply to the Screening Visit and should be ignored. Vaginal fluid pH is required at the Screening Visit per Letter of Amendment #1.

#### Social Impact Log CRF, Item 7 (current status)

Item 7, which documents the current status of the social harm, is based on participant self-report. For example, mark ‘unresolved’ if the participant reports that she feels the social harm is ongoing (not resolved). Note that SCHARP will provide sites with a monthly listing of all unresolved social harms (harms that are ongoing for more than 30 days) to help sites follow-up with participants on social harms that are ongoing

#### Vaginal Practices, item 5d

Item 5d of the Vaginal Practices CRF asks participants whether they have inserted fingers inside the vagina in order to clean or insert something. Note that this question does not include instances where the participant has used her fingers to insert a study vaginal ring.

#### CRF completion when required visit procedures are repeated at the 2<sup>nd</sup> part of a split visit

In cases where a participant has required visit procedures repeated at the 2<sup>nd</sup> part of a split visit, document the repeated procedures as an interim visit using a new Visit Summary CRF. For example, a participant has a split Month 6 visit, and at the first part of the visit on 13-NOV-12, all required procedures are completed except for the pelvic exam. At the 2<sup>nd</sup> part of her split Month 6 visit on 18-NOV-12, the pelvic is done and her safety labs are repeated in order to follow-up on an AE. The pelvic exam CRFs are assigned Visit Month 06.0. The Visit Summary for the Month 6 visit is dated 13-NOV-12, Visit Month 06.0. For the safety labs done on 18-NOV-12, assign Visit Month 06.1 to the Quarterly Lab Results CRF (date of 18-NOV-12), and complete a new Visit Summary dated 18-NOV-12, Visit Month 06.1, to document the interim visit (interim procedure is the safety lab testing).

#### Ring Adherence CRF completion at Interim Visits

Note that the Ring Adherence CRF is not completed at interim visits – only at the required Monthly, Quarterly, Semi-Annual, and PUEV.

#### Ring Collection/Insertion CRF completion for participants permanently discontinued from product use

The Ring Collection/Insertion CRF is not required to be completed once a participant has been permanently discontinued from ring use (due to confirmed HIV infection, for example).

#### Creatinine result (item2c) on Screening and Quarterly Laboratory Results CRFs

Note that per the forms instructions, only one creatinine result is recorded on the CRF (item 2c). SCHARP can only accept one creatinine result in order to properly perform our safety monitoring checks. If two creatinine results are recorded on a CRF, a QC will be created requiring you to mark



for delete (line-through) one of the results.

## Data Communiqué #2

### DOCUMENTATION OF MISSED MENSES EVENTS

#### DURING SCREENING

##### SCREENING MENSTRUAL HISTORY (SMH) CRF, ITEM 2

Item 2 should be marked "amenorrheic for past 6 months" only in those cases where the participant has been amenorrheic for the past 6 or more months. If amenorrheic for past 5 months or fewer, mark "regular" or "irregular" for item 2 based on the most recently-experience menses. In item 8, describe how long the participant has missed menses (i.e. for past 5 months, 4 months, etc.). See more information on determining start date of amenorrhea below.

#### PRE-EXISTING CONDITIONS (PRE) CRF

All instances of missed menses identified at the Screening Visit should be recorded on the PRE CRF. This is because missed menses/amenorrhea, regardless of cause or duration, is considered an irregular bleeding pattern, and as such, requires documentation as a pre-existing condition. If the amenorrhea is "expected", that is, due to hormonal contraceptive use or post-partum, the PRE entry should be marked as "not gradable". This is per the FGGT row which does not apply to cases where missed menses is due to hormonal contraception or post-partum. The cause for the missed menses should be noted in the "Comments" section of the PRE entry.

If the amenorrhea is unexplained, it should be graded per the FGGT row for "unexplained infrequent bleeding", i.e. 1-3 months in duration is Grade 1, durations of 4 months or longer is Grade 2. In "Comments" of PRE entry, note the duration. *Note that a participant with unexplained missed menses (for any duration) may indicate further review prior to enrollment into the study.*

#### Terminology

For missed menses events of 1-3 months in duration, use the term "missed menses".

For missed menses events of 4-5 months in duration, use the term "oligomenorrhea".

For missed menses events of 6 months or longer, use "amenorrhea".

#### Determining Start Date

When determining duration (start date of missed menses/oligomenorrhea/amenorrhea), use the first month of missed menses as the start. For example, if a participant's last menstrual period was in March, 2012, the start date for her missed menses is April 2012 (her next time that she would have expected menses if it had not been missed). Once the duration is established, use the guidance above to describe the missed menses event.

#### DURING FOLLOW-UP

Note that new instances of missed menses (of any duration) due to hormonal contraception use, pregnancy, or post-partum are not adverse events. These events should be documented in the participant's file but not reported on an AE Log or GAE Log CRF. This is per the FGGT row, which excludes cases of missed menses due to hormonal contraception use, pregnancy, and post-partum.

## Data Communiqué #3

#### Screening STI Test Results, item 1a (homogenous vaginal discharge)

The intent of item 1a is to document the presence of homogenous vaginal discharge in cases where the clinician is assessing for bacterial vaginosis (BV). If an assessment for BV is not done, mark "not

done”.

#### Protocol Deviation Log CRF and Participants Who Do Not Enroll

Protocol deviations are reported (using the Protocol Deviations Log CRF) for all screened participants, even if the participant does not enroll in the study.

#### Documentation When Pelvic Exam Findings are Re-assessed During Screening (prior to randomization)

If a visual exam is done after the required Screening Pelvic Exam to confirm eligibility or check on a normal (non-exclusionary) finding, completion of a new Screening Pelvic Exam CRF is not required, nor is completion of a new Pelvic Exam Checklist. A Pelvic Exam Diagrams CRF should be completed to document the assessment, and the status of the finding should be updated on either the Pre-existing Conditions CRF (for abnormal findings) or the Enrollment Abbreviated Physical Exam CRF (for normal findings). If a clinically-indicated pelvic exam is performed at the Enrollment Visit after randomization, document using a Pelvic Exam Diagrams CRF and Pelvic Exam CRF (coded 98.0).

#### Documentation of “as indicated” Physical Exams During Follow-up

Physical exams done during follow-up on an “as indicated” basis should be documented using the Abbreviated Physical Exam CRF. If vital signs (items 1-5) are not completed at an “as indicated” exam, you can line through each set of response boxes, bracket, and add a note “not done”, and initial/date the note to indicate these assessments were not done.

#### HIV Rapid Test Kit Codes on the Monthly Lab Results CRF

These codes (on the back of the MLR-1 CRF) have been updated to include a new kit code (04) for the StatPak rapid HIV test kit currently in use by the Kampala site. Kit code 01 has been updated from “Abbot Determine” to “Determine”. Kit code 02 has also been updated from “OraSure OraQuick” to “OraQuick”.

### **Data Communique #4**

#### New Protocol Deviation Log CRF (plate 495, form date of 14-NOV-12)

A new Protocol Deviation Log (PDL) case report form has been created for use in ASPIRE. The new form (PDL- same acronym as before) has several changes: for items 3 and 4, the response boxes have been changed to yes/no; item 5 is now a 2-digit code rather than a “mark only one” field. The codes for item 5 are present in the form instructions. There are 3 new protocol deviation categories present. Guidance for when to use these categories in ASPIRE is provided below.

- 05 (study product use/non-use deviation): use for cases in which the study ring has been out for more than 7 consecutive days, excluding cases in which a participant is on a clinical study product hold or has been permanently discontinued from study ring use. In addition, product non-use includes all cases in which a participant has declined study product (as documented on RCI form item 4a). Finally, for those sites not yet operating under LoA #2, cases in which a participant has had a ring in place for more than 35 days is also a reportable deviation.
- 06 (study product sharing): use when staff become aware that a participant has shared study product (used or unused) with another individual, even if the individual is an

ASPIRE participant.

- 07 (study product not returned): use when a participant does not return study product as scheduled. For example, if a participant presents for her Month 5 visit and does not bring her ring with her, report this as a deviation (even if she returns the ring at a later date). Refer to protocol Table 3 (p.29) for product retrieval requirements.

## Data Communique #5

### AE Log item 1 (AE text) and Comments field clarifications for AEs due to ring removal or insertion

The purpose of the below is to clarify information provided during study site trainings. During the trainings, we asked sites to never mention the study ring in the AE descriptive text (item 1). This guidance has been revised per the below.

- If the AE is due to the act of study ring insertion or removal, include this information in item 1. For example, use AE text of “pelvic pain due to ring removal” or “vulvar laceration due to ring insertion” rather than just “pelvic pain” or “vulvar laceration”. It is important to clearly identify in item 1 AEs that are due to the act of study ring insertion or removal, as these AEs are assigned unique coding terms within the standardized MedDRA coding system. If the AE is not due to the act of study ring insertion or removal, do not include mention of the ring in item 1.
- If text is present in the “Comments” field that the AE is due to the act of ring insertion or removal, this same text needs to be in item 1. If not, this may result in a Clinical Query asking that this information be added to item 1 so that the AE is described completely and accurately.

It is fine to include text in the “Comments” field explaining why the AE has been judged “related”, but such text is not required.

### Protocol Deviation Log (PDL-1) completion for deviations not associated with a PTID

If a deviation needs to be reported, but is not associated with a participant (for example, study product exceeds storage temperature while at the pharmacy), use a PTID that follows the format below on the PDL CRF: XXX-00000-0

The first 3 digits are the site’s DataFax ID number (312 for Kampala, for example). All PTIDs for your site start with the same 3 digits, and these 3 digits should be used (along with 0’s for the last 6 digits) for any PDL CRFs reporting non-participant related deviations. Assign page numbers sequentially (as usual) when completing new PDLs using this PTID.

### Product Hold (PH-1) and Vaginal Ring Request Slip completion in cases where a participant is requested to remove the ring due to more than 35 days of use

If a participant is requested by study staff to remove the ring to avoid more than 35 days of continual use, complete a new PH-1 form and Vaginal Ring Request Slip to document this requested hold. It is expected these requests will not be made once a site is operating under Letter of Amendment #2.

On the PH-1 form, mark item 2 as “other” and specify that more than 35 days of use as the reason for the requested hold.

On the Vaginal Ring Request Slip, mark “hold” and specify the text above. Note that for the next

ring dispensation for the participant, you will need to mark “resume” on the slip.

#### Participant report of shorter than usual menses during follow-up

Note that reports of shorter menstrual periods during study follow-up (which may be a change from the participant’s baseline bleeding pattern) are not adverse events and do not get reporting on AE Log CRFs.

### **Data Communiqué #6**

#### Concomitant Medications Log – Frequency and Route

Note that if “once” is marked for a medication’s frequency, both a Date Started and a Date Stopped must be present, and these should be the same date.

When recording intra-uterine contraceptive devices or contraceptive implants, record the date of insertion as the Date Started, and leave the Date Stopped blank (record a Date Stopped once the device or implant is removed). Mark “other, specify” for frequency and on the line provided, specify “continuous” as the frequency. When recording contraceptive implants, mark “other, specify” for route and on the line provided, specify “sub-dermal”.

#### Grading of menorrhagia, metrorrhagia, and menometrorrhagia at Baseline

Note that any menorrhagia, metrorrhagia, or menometrorrhagia events ongoing at the time of randomization are marked as ‘not gradable’ on the Pre-existing Conditions (PRE) CRF. This is because the FGGT grades 1-4 for these events (see rows below) are relative to each participant’s baseline (day of randomization) status. In the “Comments” field of the ongoing PRE entry, include text similar to what is in the FGGT row to describe the severity/frequency. For example, for an ongoing event of menorrhagia, mark “not gradable” and in the PRE Comments, record “no interference with ppt’s usual activities” (similar to text used in the FGGT to describe Grade 1). Adding such text to the Comments field will help ensure that increases in the severity or frequency of these events compared to the participant’s baseline status are easily identified (and reported as AEs on an AE Log CRF). Refer to SSP Section 10.6.1 as needed.

Any resolved (not ongoing) menorrhagia, metrorrhagia, or menometrorrhagia events documented on the PRE CRF should be assigned a grade from 1-4 per the FGGT.

### **Data Communiqué #7**

#### Revised Ring Collection/Insertion (RCI-1) case report form

In an effort to obtain more data on ring use, a new item, item 7, has been added to the RCI-1 CRF. The intent is to have this item (“Appearance of most recently-used ring) completed by site staff each time the RCI-1 is completed. If no used ring was returned at the visit (item 2 is “none”, then item 7 is still completed. In this case, item 7 is marked “no ring”.

Note that the skip instructions off of items 4a and 6 (for the “yes” response) have been updated to direct you to item 7, as item 7 should be answered even if item 4a is completed or item 6 is “yes”. If more than one used ring is returned at a visit, item 7 should be answered based on the appearance of the most recently-used ring. This item should be answered based only on the

appearance of the ring – do not include factors such as self-reported ring use or other information when answering this item. Please see the form instructions for this item for these and other clarifications related to this new item.

The site-ready version of the revised RCI-1 CRF (form date of 27-Feb-13) is provided with this communicate, and is also available via the CRF packets and “As Needed” pdf files on the MTN-020 Atlas web page.

We ask that by March 19, 2013, all sites print out the revised CRF and use it to replace all unused current versions of the RCI-1 CRF present in participant study binders and unassigned follow-up visit packets (Monthly, Quarterly, Semi-annual, PUEV, Early Termination). Starting on March 20, 2013, we will expect to only receive the revised RCI-1 form for visits completed on this date forward.

### **Data Communiqué #8**

#### AE and GAE Log CRF Revisions (Revised forms dated 26-APR-13)

Protocol Team leadership has determined it is valuable to capture the rationale for both related and not related “relationship to study product” assessments when documenting adverse events (AEs). As such, item 4 of the AE and GAE Log will be revised so that there is no longer an arrow off of the “not related” box. When completing item 4 (relationship to study product) of the revised AE and GAE Log, a rationale should always be recorded (the “Record rationale” is a required field on the revised CRF). If the “Record rationale” field is left blank, this will result in a QC. Guidance on what type of information to record in the “Record rationale” field will be provided separately by the Protocol Safety Physicians.

For AEs already reported, SCHARP will follow-up with sites individually on needed form additions. The goal is to have sites add text to the “Record rationale” field for all previously-reported grade 2 and higher related AEs.

The updated versions of the revised AE and GAE Log CRFs are provided with this communiqué, and are also available via the CRF packets and “As Needed” pdf files on the MTN-020 Atlas web page.

#### HIV Confirmatory Results (HCR-1) CRF Revision (Revised form dated 26-APR-13)

An error has been identified on the HCR-1 CRF. The original form listed a “GP40” band in item 2. This should have read “P40”. The revised form, dated 26-APR-13, lists the correct P40 band. No action is needed on HCR-1 forms already submitted, as any information recorded in the row for the GP40 band will be reported as the P40 band.

The updated version of the revised HCR-1 CRF is provided with this communiqué, and is also available via the CRF packets and “As Needed” pdf files on the MTN-020 Atlas web page.

#### New Prevention Study Experiences (PSE-1) CRF

A New Prevention Study Experiences case report form has been created for use in ASPIRE. This new interviewer-administered form includes additional acceptability questions on the participant's perception of product efficacy and her product assignment, and assesses her understanding of the study randomization process. Completion of this form is required at all future Month 3 and Month 12 visits. This form should *not* be completed in retrospect for Month 3 and Month 12 visits that have already been completed or missed. In addition, it should not be completed for those Month 3 and Month 12 visits that occur after a participant has been confirmed as an HIV seroconverter based on protocol algorithm testing.

The site-ready English version of the PSE-1 is provided with this communiqué. SCHARP will e-mail sites to work on translation of this form and translated versions of this form will be added to the interviewer-administered visit-based packets on the MTN-020 Atlas web page when finalized.

#### Ring Adherence (RA-1) CRF, item 5

When completing item 5 (reasons vaginal ring was out) which is a “mark all that apply” item, please keep in mind the following.

- For 5a, “ring caused discomfort”, mark this box (and not 5m) if the participant reports experiencing genital or other symptoms that caused her to remove the ring. If you wish to provide more details, these details can be added in the Comments field at the bottom of the page (these additional details are not required, however).
- For 5d, “had or was expecting menses”, mark this response if the participant removed the ring due to any type of genital bleeding or spotting (not just menses).
- Only mark 5m “other, specify” if the reason the participant removed the ring is not already listed. If you wish to provide additional details on an item that is marked among 5a-5l, use the Comments field at the bottom of the page.
- Only mark 5t “other, specify” if the reason the ring came out on its own is not already listed. If you wish to provide additional details on an item that is marked among 5n-5s, use the Comments field at the bottom of the page.

### **Data Communiqué #9**

#### Ring Adherence (RA-1) CRF, version 1.0 (version date: 30-JUL-13)

The RA-1 CRF was updated as follows:

- a. The item 4 text “In the past month” was added to clarify the time frame in question.
- b. Item 5 response boxes were replaced with Reason Code boxes.
- c. The form instructions in the General Information/Instructions, item 1, and item 2 sections were updated to clarify the intent of data capture, based on common site e-mail queries received to date.
- d. Reason Codes were added to the item 5 form instructions, and bolded lead-in text was added to the reason text.
- e. Reason Codes for ring removals were grouped into categories (Hygienic or Physical Reasons, Social or Sexual Reasons, Study-related or Procedural Reasons).
- f. The text for Reason Codes 10 and 14 was amended to incorporate language from Data Communiqué # 8.
- g. Additional reasons were added (Reason Codes 13, 15, 16, 23, 27, 28, 32-34) based on a review of common “other” site responses to date.

A separate document, entitled “MTN-020 Ring Adherence CRF: Item 5 Reason Code List”, has been developed to aid site staff in completing item 5 during participant interviews. The document has been posted on the MTN-020 Atlas page in the “Visit Packets and All CRFs” section under “Other Documents”. Site staff are encouraged to print this document and have it available for reference when completing the RA-1 CRF.

The visit packets posted on Atlas have been updated to include this new version of the RA-1 CRF. Sites may begin transitioning to use of this new version immediately. The old version of the form may continue to be used until **Aug. 12, 2013**, at which time all **sites are expected to use the new version exclusively**.

### Ring Worries (RW-1) CRF – Item 3

If a participant permanently discontinues study product prior to the scheduled PUEV, complete all items on the Ring Worries CRF, including item 3, at the permanent discontinuation visit instead of at the PUEV.

### Updates to AE Log (AE-1)/ Grade 1 AE Log (GAE-1) CRFs – Item 4 Rationale

If a previously completed GAE/AE Log CRF page is updated with new information (such as any medications taken for the AE, or a change to product relatedness), review the other items on the page for consistency and update responses as appropriate. In particular, if the AE relationship to study product changes due to test results that confirm a diagnosis, update both item 1 and item 4.

Example: An AE is reported as “vaginal discharge” per participant report in Item 1, and deemed ‘related’ in Item 4 with the rationale that the discharge presented after the participant started using the ring. Subsequently, she tested positive for Trichomoniasis. The AE Log page was updated from ‘related’ to ‘not related’ in Item 4. The rationale was updated to document the presence of an STI. In this example, Item 1 should also be updated to reflect this new information and accurately report on the presence of an STI (i.e., line through “vaginal discharge” and record “vaginal trichomoniasis”). **Discordant text in Item 1 and Item 4 will result in a QC.**

### Concomitant Medications Log (CM-1) CRF – Coding Queries

If possible, record the trade name of a medication on the CM-1 log CRF. If a trade name is not available or not reportable per national guidelines, please record the generic name of the medication. A combination medication can be recorded as one entry using the generic name.

If a combination medication does not have a generic name, or the generic name is unknown, **each** active ingredient must be reported as a separate entry in order to be accurately coded at SCHARP.

Example: A combination medication with an unknown generic name and active ingredients Chloramphenicol and Dexamethason should be recorded as two separate entries on the CM-1; one entry for each active ingredient.

Minor spelling differences can affect the coding of these medications. Please ensure that the spelling of medications is both correct and consistently used throughout the study. For example, if a medication has multiple accepted spellings (such as Azithromycin Mylan and Azithromycine Mylan), be sure to use consistent spelling at each site throughout the study.

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

Mark 'participant declined study ring' if the participant declined the study ring herself or if the participant declined the study ring due to the wishes of her family or friends.

#### Product Hold Log (PH-1) CRF – Item 4 'early termination' response

If a participant terminates early from the study and the site has placed the participant on a clinical product hold that has not yet been resolved (i.e., Item 4 on the PH-1 CRF has not yet been completed), mark "no-early termination" as a response to Item 4 and enter the participant's termination date in the corresponding date boxes.

### **Data Communiqué #10**

#### HIV and AE Reporting

HIV acquisition (seroconversion) is one of the study primary endpoints, and is thus not considered an AE for data collection or reporting purposes. "HIV infection" should not be reported as an AE or written anywhere on an AE/GAE Log CRF.

However, primary HIV infection is often symptomatic, and a constellation of symptoms may best be summarized as primary HIV infection illness. In this case, as in other cases when symptoms are best expressed as a unifying diagnosis, it is important to use that summary diagnosis. Thus, if a participant seroconverts and develops one or more signs or symptoms of acute HIV-infection, it is appropriate to report these sign(s)/symptom(s) as a single AE using ONLY the term "seroconversion illness" for item 1 on the AE/GAE Log CRF. Use the comments section of the AE/GAE Log CRF to describe each HIV-related sign/symptom (e.g., fatigue, pharyngitis). On the Rationale line for item 4, record "acute HIV". To avoid generating a QC for item 4, please ensure that the term "acute" is included.

Complete the other items on the AE Log CRF per the general form instructions. The onset date in item 2 should be completed using the date on which the participant first reported experiencing the first sign/symptom of acute HIV-infection. If there is more than one HIV-related sign/symptom, record the highest severity grade in item 3. A seroconversion illness AE is considered 'resolved' (item 6) when all of the associated signs/symptoms have resolved or returned to baseline per participant report, and medications for the symptoms are no longer indicated. In item 7, mark any medications indicated and taken for the associated symptoms, if applicable.

If one or more signs/symptoms, reported on separate AE/GAE Log pages, are later attributed to acute HIV-infection, change the earliest reported sign/symptom page to the "seroconversion illness" diagnosis and list any other signs or symptoms in the comments section of this AE Log page. In addition, mark the AE/GAE Log pages for the other signs/symptoms, if any, for deletion and write at the top of the page, "Delete due to diagnosis on AE Log page (insert page #)".



Please note that this represents new reporting guidance that is considered in effect for all new AEs reported after the date of this communiqué. It is not necessary to review or modify previously reported AEs to comply with this new guidance.

#### Specimen Storage (SS-1) CRF Required at Monthly Visits for Used Vaginal Ring Collection

The Specimen Storage CRF is required at monthly visits for collection of the used vaginal rings, beginning at each specified site implementation date. This form should be completed for all study participants.

Mark item 4 (used vaginal ring collection) “not required” for participants on temporary product holds and those participants who have been permanently discontinued from study product. If ring collection was required per protocol, but was not stored for whatever reason, mark “not stored” and indicate the reason that the ring was not stored on the adjacent line. Possible reasons include but are not limited to the following examples:

- participant forgot to return the ring to the clinic or
- ring was lost
- participant declined ring at previous visit
- ring had recently been inserted at an interim visit (and she was not getting a new ring at this visit)
- any other reason that a ring was not available to collect at the participant’s regularly scheduled visit.

#### Concomitant Medications (CM-1) Log CRF – coding queries

Household products should not be reported as concomitant medications on the CM-1 log CRF. Examples of household products that are not considered concomitant medications include cleaners, solvents, or Coca Cola used for at-home douching, saline sitz baths, and saline gargles.

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

If a medication’s trade or generic name is unknown, record “unknown” and a description or drug class.

Examples: “unknown white tablet”, “pink and white tablet name unknown”, “unknown analgesic”, “antibiotic unknown”

### **Data Communiqué #11**

#### HIV Confirmatory Test Results CRF (HCR-1)

If item 5 on the HCR-1 CRF is marked as ‘pending’, this item must subsequently be updated with the participant’s final serostatus (HIV-infected or HIV-uninfected) once confirmatory testing has been completed. Review all HCR-1 CRFs that have been completed thus far during the study and update as needed.

Example: A participant's HIV rapid tests results are both positive at her Month 5 visit on 14February and her Western Blot is indeterminate. Item 5 on the HCR-1 CRF is marked as 'pending' while further testing is completed. On 10March, her repeat Western Blot result is positive and item 5 on a second HCR-1 is completed as 'HIV-infected'. At this point, Item 5 on the HCR-1 CRF, dated 14February, should be updated to "HIV-infected" and the 'pending' box should be lined through with all changes dated and initialed prior to refaxing to SCHARP.

### Concomitant Medications Log CRF (CM-1)

All contraceptives that are dispensed to a participant, regardless of indication, should be recorded on the CM-1 Log CRF with the item "If contraceptive, was it dispensed at the research center?" completed. This item should be completed if a contraceptive is dispensed to a participant even if it is for reasons other than family planning (e.g. to treat an AE) and marked 'yes' if dispensed at the research site.

Combined OCP pill packs that contain multiple ingredients should be recorded as one entry on the CM-1 Log CRF with the trade name provided, if possible. For example, if a participant is using Microgynon as her current contraceptive method, complete one entry per pill pack. Placebo ferrous fumarate pills should not be listed in a separate entry.

### **Data Communiqué #12**

#### **New Study Exit Behavior Assessment (SEV-1~5) and Social Influences Assessment (SOC-1)**

New Study Exit Behavior Assessment (SEV-1) and Social Influences Assessment (SOC-1) case report forms have been created for use in ASPIRE.

The Social Influences CRF will be administered at the scheduled Product Use End Visit (PUEV) and includes questions regarding the participant's social influences on study participation and ring use.

The SEV-1~5 CRF will be administered at the participant's scheduled Study Exit/Termination Visit and includes questions on participant sexual activity, condom use, intravaginal practices and behavior change after participants have completed study product use.

The site-ready English language versions of the Study Exit Behavior Assessment CRF and the Social Influences Assessment CRF are provided with this communiqué. SCHARP will work with sites to create site-specific language versions of each CRF, which will be posted in the "Interviewer-administered Visit-based Packets" pdf files on the Atlas MTN-020 web page, once finalized.

#### **Genital Bleeding AE Reporting in the Context of Contraceptive Switches**

This guidance applies to cases where a previously reported genital bleeding event, such as metrorrhagia, is ongoing and persists even after a participant has switched her method of contraception. This applies to contraceptive switches within the same class (e.g., from one type of injectable to another type of injectable) or between different classes of contraceptives (e.g., from an injectable to an IUCD). If the bleeding event persists at the same severity and frequency despite the change in contraceptive use, the AE should be left open and considered ongoing. If the event is deemed “not related” to study product use, sites can simply state on the item 4 “Record rationale” line, “consistent with contraceptive use”. A new AE Log CRF should not be completed, as the switch in contraceptive use has not caused a new bleeding event at a different severity or frequency to occur. One AE Log CRF suffices to cover the same bleeding event if it persists even with a switch in contraceptive method.

Please apply this guidance going forward. It is not necessary to conduct a retrospective data review to ensure compliance with this guidance.

### **Completion schedule of the Seroconverter Laboratory Results CRF (SCR-1)**

The Seroconverter Laboratory Results CRF documents CD4+ and HIV RNA test results, MTN-015 enrollment status, and seroconverter plasma storage for participants who have been confirmed as HIV-1 infected (i.e., with a final HIV status of “HIV-infected” per the HIV Confirmatory Results CRF).

This form should be completed at scheduled ASPIRE study visits occurring 1 month, 3 months, 6 months, and every 6 months thereafter post HIV infection and should be completed for all participants, regardless of enrollment status in MTN-015. Please refer to the MTN-020 Seroconverter Specimen Collection Tool on the study webpage to determine participant-specific seroconverter specimen scheduling.

Example: A participant’s HIV rapid tests are both positive at visit month 7.0. Her Western Blot is also positive.

- Documentation at Visit Month 7.0
  - i. Monthly Laboratory Results (MLR-1) CRF is completed to document the HIV rapid test results and storage of confirmatory plasma.
    - a. Confirmatory plasma storage corresponds to the LDMS primary specimen “Plasma for HIV Seroconversion Confirmation” with the other specimen ID field labeled with “CON”
  - ii. HIV Confirmatory Results CRF is completed with a final HIV status of “HIV-infected” when confirmatory testing results are available

*Note: The SCR-1 CRF should not be completed at visit month 7.0.*

- Documentation at Visit Month 8.0
  - i. Complete SCR-1 to document MTN-015 enrollment status, testing results, and seroconverter plasma storage.
    - a. Seroconverter plasma storage corresponds to the LDMS primary specimen “Seroconverter Plasma Storage” with the other specimen ID field labeled with “SER”
  - ii. Mark Item 4 “*Was plasma stored for HIV confirmatory testing?*” on the MLR-1 form as “Not required”

The SCR-1 CRF should be completed for this participant at study visits 8.0, 10.0, 13.0, 19.0 and every six months thereafter.

### Data Communiqué #13

#### AE Outcome Date when treatment is indicated

For adverse experiences requiring treatment, record as the outcome date the date when all associated symptoms have resolved (or returned to baseline severity), or the date when treatment is completed, *whichever is later*. An AE is not considered resolved until both symptoms have resolved and treatment has been completed.

**Example:** A participant presents with Grade 2 vaginal discharge on 23May14 and is prescribed doxycycline on the same date. The participant's symptoms resolved on 27May14 and she completes her antibiotic regimen on 06Jun14. The outcome date recorded in item 6 on the corresponding AE log page CRF should be 06Jun14.

#### Assignment of AE severity grade for genitourinary infections and symptoms

If an AE is graded using the 'general infection' row of the DAIDS Toxicity Table and requires systemic antimicrobial therapy, the infection must be graded automatically at Grade 2 or higher. Please refer to SSP Section 11.4 for this guidance. However, if a genitourinary AE is treated with systemic antimicrobials, the severity grade will depend on whether the Female Genital Grading Table (FGGT) or the main DAIDS Toxicity Table is used to grade the AE. For AEs graded according to the general "infections" row of the main DAIDS Toxicity Table, treatment with systemic antimicrobials warrants a severity grade of 2 or higher. For AEs graded according to the FGGT, treatment with systemic antimicrobials may still be covered under severity grade 1; grading will depend on the criteria defined in the given row.

**Example #1:** A participant presents with mild vaginal discharge and itching. Wet mount test results are positive for candida and she is given a dose of Fluconazole for treatment. This genitourinary infection should be graded as Grade 1 per the criteria of the Candida row of the FGGT regardless of whether an antimicrobial was prescribed.

**Example #2:** A participant presents with nasal congestion, fever, and headache consistent with infective frontal sinusitis and is prescribed Augmentin to treat the infection. Per the general infection row of the DAIDS Toxicity Table, this AE should be reported as at least Grade 2, since systemic antimicrobial treatment was indicated.

#### Documentation of Missed Menses Events during Follow-Up

Adverse Events for missed menses that extend beyond three months or more in duration should be documented by updating the completed AE log CRF for “missed menses” with a new AE term of either “oligomenorrhea” (for missed menses events of 4-5 months in duration) or “amenorrhea” (for missed menses events of 6 months or longer) and with a new severity grade. The updated AE term and severity grade should be assessed per the FGGT row for “unexplained infrequent bleeding”, which excludes cases of missed menses due to hormonal contraception use, pregnancy, or post-partum. A new AE log CRF should not be completed to document an increased duration of the same infrequent bleeding event.

**Example:** A participant experiences unexplained infrequent bleeding for two months and an AE log CRF for grade 1 “missed menses” is completed. She continues to miss her menses for two subsequent months (for a total of 4 months duration). At this point, Item 1 on the AE for ‘missed menses’ should be updated to reflect the updated AE term “oligomenorrhea” with an updated severity grade of 2 (Item 4). If this participant continues to experience missed menses for an additional two months or more, the AE log CRF should be updated once again to reflect the new AE term, “amenorrhea”.

#### Cervical Ectopy Assessment

Cervical ectopy is considered to be neither a normal nor an abnormal finding, but rather, is a required separate assessment. The percentage of cervical ectopy (item 3) on the PE-1 CRF should always be completed when a pelvic exam is conducted. However, the ‘no normal variants or abnormal findings’ box on the pelvic exam diagrams non-DataFax form may be marked if only ectopy is observed. The presence of cervical ectopy is quite common, and should not be factored into the question on the diagrams form.

#### CRF Tracking Reports

The CRF Tracking System (CTS) provides feedback, via emailed reports, to help sites track the number of CRFs that have been received and validated at SCHARP. There are two types of reports – a Reception Report and a Validation Report. A Reception Report is a listing of transmissions received from a site’s registered devices/email addresses and includes the date and time each transmission is received, the number of pages received and a unique “Fax “Raster” ID. A Validation Report lists the Study, PTID, Fax ID page number, CRF plate number, visit code, and validation date for each CRF received at SCHARP.

Sites can manage the frequency of and staff distribution lists for these reports by emailing the CTS administrator at [support@scharp.org](mailto:support@scharp.org) and completing or updating a CRF Tracking System Registration Form. Note that the registration form must be faxed from all devices or email addresses used to transmit CRFs to SCHARP.

### **Data Communiqué #14**

#### Ring Adherence (RA-1) CRF, item 4

In item 4 of the Ring Adherence CRF (version 1.0), provide the longest number of days in a row the vaginal ring was out during the *past study month*. If a participant missed her previous visit and was not dispensed an additional ring, the target date of that missed visit should be used when calculating the number of days the ring was out.

Example: A participant misses her Month 7 and 8 visits. Her Month 8 visit target date was on 08Oct14. She returns for her Month 9 visit on 10Nov14 with a used vaginal ring and reports that she removed the ring on 07Sep14. To complete item 4 on the RA-1 CRF, calculate the number of days the ring was out using the last missed visit's target date, in this case 08Oct14. In other words, report in Item 4 that the ring was out for the past 34 days (the amount of days between 10Nov14 and 08Oct14).

The Ring Adherence CRF should be completed at scheduled monthly visits only. This form should not be completed at interim visits. If a participant has an interim visit between study visits, chart note any outages that the participant has had in order to provide a complete recording of ring outages for the entire previous study month.

#### **14.5 Case Report Forms**

The current version of the MTN-020 case report form can be found at the top of the MTN-020 SSP web page, link provided below.

<http://www.mtnstopshiv.org/node/3620>