

Section 13. Data Management

This SSP section describes general data management requirements for MTN-016, including how to complete, store, and transmit case report forms using DataFax, the system for data management used by the Statistical and Data Management Center (SDMC) for this study. This SSP section should be used in conjunction with DAIDS and study site SOPs when reviewing all aspects of data management related to MTN-016. For questions about this section or about general data collection policies, procedures, or materials, please contact the MTN-016 Project Manager.

For this study, the SDMC is SCHARP (the Statistical Center for HIV/AIDS Research and Prevention). SCHARP is located in Seattle, WA, USA, and is in the US Pacific Time (PT) time zone. The SCHARP MTN-016 team members, along with their job roles and e-mail addresses, are listed below.

Role on MTN-016	Name	E-mail address
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13.1 DataFax Overview

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

Case report forms can be transmitted to SCHARP DataFax in one of two ways:

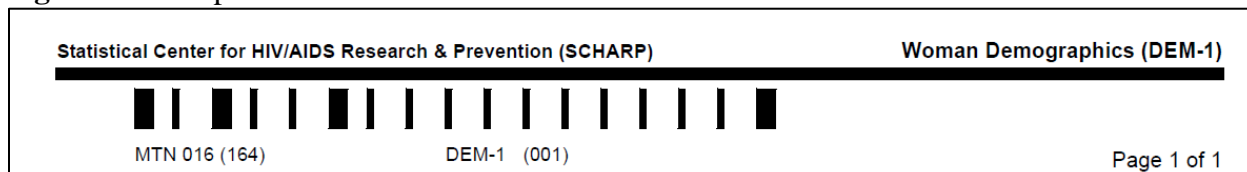
1. faxed using a fax machine connected to a land phone line (**fax to phone number 206-667-4805**) or
2. faxed using a fax machine connected to the internet (**fax to e-mail <datafax@scharp.org>**). ***This is the preferred method of transmission.***

SCHARP's Technology Systems and Services (TSS) group is available to consult with the site to determine the best method for data transmission. The SCHARP TSS group should be contacted (**support@scharp.org**) anytime the site has technical questions or problems with their fax equipment.

13.1.1 Receiving CRFs

Once a CRF image is received by SCHARP DataFAX, DataFAX identifies the study to which each CRF belongs using the barcode at the top of the form (**Figure 1**). Thus, it is important to not obscure, mark over, or punch holes through this barcode.

Figure 1: Example of Barcode



DataFAX reads the data using Intelligent Character Recognition and transfers the data into the appropriate study database. DataFAX processes images by separating a fax into individual pages, adjusting each page to correct for proper alignment and rotation.

13.1.2 Quality Control

Each CRF is reviewed by at least two members of SCHARP's Data Operations Group. Problems such as missing or potentially incorrect data (for example an out-of-range value) are identified and marked with a Quality Control (QC) note. **[Please note:** CRFs will only show up on a QC Report once this review stage has been completed by SCHARP staff, even though CRFs may have already been received by DataFAX.] QC notes are then compiled into QC reports that are e-mailed to the study site on a regular basis. The QC report will also show information on missing pages and overdue visits. For more information on QC reports see SSP Section 15.

13.1.3 Anatomy of a QC Report

The first page of every QC report is the cover letter, written to the site by the SCHARP Data Coordinator. The cover letter serves the following purposes:

- identifies the QC report on the following pages,
- alerts the site to trends in data quality that may need attention, and
- lists the individuals to whom the QC report is being sent (this includes site staff and SCHARP staff).

The second page of the QC report begins with the Fax/Refax List, which lists the QCs. Typically QCs are sorted by participant ID. Each QC note includes the following:

- participant ID
- visit code (or page number, if the CRF is a log form)
- CRF acronym
- query text (if needed)

- value that was written on the CRF by the site (if present)
- QC problem type

The QC report may also contain a Question and Answer (Q&A) List. The Q&A List includes QCs with extra space for site staff to translate the QC into their local language. These Q&A QCs may also be used to describe more complex QC issues.

13.1.4 Resolving QCs

Upon receipt of the QC Report from SCHARP, site staff should review the report and correct and/or clarify data on the study CRFs. The revised CRFs (but not the QC Report itself) should be retransmitted to SCHARP DataFax as soon as possible. Once received, an additional electronic copy of the CRF is saved in the DataFax database and SCHARP staff review the newly corrected pages and resolve the QCs. If corrected CRFs are not received and entered by SCHARP before the next QC report is generated by the Data Coordinator, the QC note(s) may appear again on subsequent QC Reports.

If a change is made to a CRF but the updated page is not retransmitted to SCHARP DataFax, the change will not be reflected in the database and the study database will continue to contain incomplete or incorrect data. Therefore, it is very important that the site retransmit updated CRF pages to SCHARP DataFax **any time** a change is made to data, regardless of whether or not the change was made in response to a QC report.

Periodically a Data Management Quality (DMQ) Report will be shared with the study team. This “QC metric” report includes overall information on a site’s data management performance, such as average number of days to fax in CRFs, total number of QCs identified, and percent QCs resolved. See SSP Section 15 for more information.

13.2 Case Report Forms (CRFs)

13.2.1 CRF Distribution

Case report forms can be distributed as pdf form sets or CRFs can be printed at SCHARP and mailed to sites. For MTN-016, the forms live on SCHARP’s web-portal, Atlas:

<https://atlas.scharp.org/cpas/project/MTN/016/begin.view?>

The forms are organized by visit and appear as “visit packets”. Each visit packet contains all of the required CRFs for the visit. For example, the Woman Screening and Enrollment packet includes all CRFs listed for this visit in the Case Report Form Completion Schedule – Women table (Table 13-5). In addition to form packets, bulk supplies of “as needed” CRFs are also located on Atlas (for example, Woman Subsequent Consent, Infant HIV Test Results, Social Harms Assessment Log, etc.).

Sites can download and print the forms whenever they need them. Printing instructions are included on Atlas, in the “Other Documents” section.

13.2.2 Updating Individual CRFs or Form Sets

If it becomes necessary to modify or add an individual CRF or entire form set after it has been released to the sites, SCHARP will make the revision, change the version date on only the specific CRF with the edit, and update all affected form sets with the modified CRF. SCHARP will email the sites once the updated forms or form sets are available. The site must destroy all unused copies of the old version of the form.

13.2.3 Standard CRF Elements

Most case report forms contain standard CRF elements such as a line for recording staff initials and dates, and boxes for recording participant identification numbers, visit codes or page numbers. The format of these elements may vary from study to study, so it is important to pay attention when completing these items. An explanation of the standard CRF elements can be found below.

13.2.4 Staff Initials and Date

Every DataFax CRF includes a line in the lower-right corner of each page for a staff member’s initials and the date when the form was completed. The site staff person who initially completes the form must record his/her initials and the date in the space provided. 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 should write his/her initials and date next to each data element for which he/she is responsible. It is acceptable to bracket a section an initial and date once for that entire section.

13.2.5 Participant IDs

DataFax uses a unique participant identification number (PTID) to identify each study participant in the database. SCHARP provides each site with a list of PTIDs prior to study start-up. The site should assign one PTID to each study participant enrolled in the study. Site staff are responsible for maintaining a log linking PTIDs to participant names (PTID-Name Link log) in accordance with Section 3 of this manual.

The PTIDs should be assigned in sequential order, and the site should ensure that each PTID is only assigned once. Once a participant has received a PTID, she maintains the same PTID throughout the entire study. Specific procedures for assigning PTIDs (who will assign the PTIDs, where the PTID-name log will be stored, etc.) should be noted in the site’s Data Management SOP.

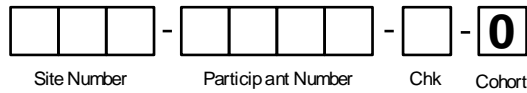
PTID boxes are located near the upper left corner of each DataFax CRF. On multiple page CRFs, the PTID must be filled in on each page.

The PTIDs used for this study are nine digits and formatted as “WWW-XXXX-Y-Z.” The PTID consists of four parts: the site number (WWW), the participant number (XXXX), a numerical check digit (Y) and the cohort number (Z). The check digit (Y)

is a number generated by SCHARP along with the participant number (XXXX), and helps ensure that the correct PTID is recorded. The cohort number (Z) is used to identify each participant as the woman (0) or infant (1, 2, 3, etc.)

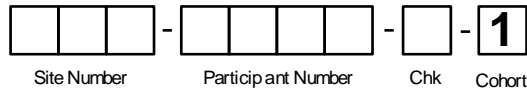
Below are examples of the PTID structures used in MTN-016.

Mother Participant ID



The cohort number for women will always be “0.”

Infant Participant ID



The Infant PTID is identical to its mother’s PTID with the exception of the last digit, the cohort number. For infants, the cohort number will be 1, 2, 3, etc. For the first infant born **and enrolled** to a woman enrolled in MTN-016 the cohort number will be “1.” For the second infant born **and enrolled** to a woman enrolled in MTN-016 the cohort number will be “2.” If the woman (for example, PTID 301-1234-9-0) has multiple infants throughout her enrollment in MTN-016, but only chooses to enroll the 1st and 4th born, the PTIDs for the enrolled infants will be 301-1234-9-1 and 301-1234-9-2, respectively.

13.2.6 Visit Codes

DataFax CRFs usually include boxes in the upper right corner for a visit code. DataFax uses this number to identify the visit at which the CRF was completed.



However, not all CRFs include boxes for visit codes. If a form is only completed and transmitted once during a study (e.g., the Woman Demographics CRF), no visit code box will be provided; the visit code will be automatically assigned by DataFax.

Please remember: For specimen collection, the visit code and date on the CRF must match the visit code and date in the LDMS database.

All study visit codes for MTN-016 are listed in the table below (**Table 13-1**).

Table 13-1: MTN-016 Visit Codes

	Study Visit	Visit Code
MOTHER	Screening and Enrollment	1.0
	Quarterly Visit #1	2.0
	Quarterly Visit #2	3.0
	Quarterly Visit #3	4.0
INFANT	Newborn/Initial Visit	1.0
	Month 1 Visit	2.0
	Month 6 Visit	3.0
	Month 12 Visit	4.0

13.2.7 Page Numbers

Some CRFs, such as log forms (e.g., Social Harms Assessment Log), may include boxes in the upper right corner for page numbers, as shown below:

Page

--	--

Page numbers should be assigned in sequential ascending order, starting with 01, and should never be changed unless instructed by SCHARP. In the example of the Social Harms Assessment Log, the participant’s first social harm reported would be page 01, the second social harm reported would be 02, etc. This numbering is followed throughout a participant’s entire duration in the study, regardless of the visit when the social harm is reported.

Note: For multiple pregnancies, **do not restart page numbering with a subsequent consent (i.e. pregnancy cycle)**. For example, if a participant reported 2 separate social harms (pages 01 and 02) during her first pregnancy, and then during her second pregnancy she reports another social harm, the newest social harm will be page 03. Please see section 13.6.1 for more information on pregnancy cycles.

13.2.8 Pregnancy Number

Some CRFs for Women in MTN-016 also include boxes in the upper right hand corner for the pregnancy number, as shown below:

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Pregnancy #

Pregnancy number is synonymous with *pregnancy cycle* (see section 13.6.1). Women in MTN-016 may have multiple pregnancy cycles; that is a woman may have more

than one eligible and enrolled pregnancy during her participation in MTN-016. The first enrolled pregnancy will be Pregnancy Number 01. The next eligible **and enrolled** pregnancy will be Pregnancy Number 02, etc. If the woman participant has multiple pregnancies throughout her enrollment in MTN-016, but only chooses to consent for her 1st and 3rd pregnancies, the Pregnancy Numbers for the eligible and enrolled pregnancies will be 01 and 02, respectively. The CRFs for the infant participants do not include the Pregnancy Number.

13.2.9 Outcome Number

On the Pregnancy Outcome CRF you will also find a box for an “Outcome Number”. The outcome number refers to the number of outcomes from any given pregnancy. A pregnancy outcome can be an infant or a fetus. For a single baby or fetus, the outcome is 1. The conception of twins will result in two outcomes. See the instructions on the back of the Pregnancy Outcome CRF for more information.

13.2.10 Non-DataFax CRFs

For some studies, the site may receive non-DataFax forms from SCHARP (e.g. the Woman Medical History Log). These forms will be easily identifiable because there will be no barcode along the top of the CRF. In place of the barcode, the following text will appear: “Not a DataFax form. Do not fax to DataFax.”

These forms should **not** be transmitted to SCHARP DataFax. Instead, they should be kept in the participant’s file as a record of the activities recorded on the form. When applicable, the guidelines described above for all CRFs should also be applied when completing non-DataFax CRFs as well.

13.2.11 Form Storage

Specifications for form storage will be detailed in the site’s MTN-016 Data Management SOP. It is recommended that, for each participant, study CRFs be stored in a hard-cover notebook. SCHARP can provide a template for use in creating notebook cover labels and spine labels and can also provide a template that can be used to create tab dividers.

It is suggested that Concomitant Medications Log forms 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.

13.2.12 Printing CRFs

CRF printing instructions are included on the MTN-016 Atlas home page: <https://atlas.scharp.org/cpas/project/MTN/016/begin.view?>

DO NOT PRINT CRFS ON COLORED PAPER. Certain colors of paper do not transmit well, thus making it difficult for DataFax to read the data from those CRFs into the database.

13.3 CRF Completion Guidelines

13.3.1 General Guidelines

Based on the use of electronic transmission of case report forms and Good Clinical Data Management Practices (GCDMPs), the following guidelines should be used for completing DataFax CRFs:

1. Read and follow all form instructions carefully.
2. Use a black or dark blue medium ballpoint pen. Do not use any other type of writing tool.
3. Use only one color pen 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.
4. Press firmly when recording data or writing comments.
5. Print all data and comments legibly by hand.
6. Do not use cursive/script handwriting, as it can be difficult to read.
7. Write numbers as large as possible while staying within the boundaries of the boxes.
8. Use the units of measurement that are requested on the form.
9. Record data on the front of CRFs only. DataFax cannot read the back of CRFs.
10. Record a response for every item unless instructed otherwise by a skip pattern.
11. Record responses and comments in English, unless stated otherwise.
12. If the lines provided for written responses are not long enough, continue in another blank area of the form (within the page margins).
13. Mark only one answer except when given the instruction “Mark all that apply.”
14. In general, do not record data or make marks in the margins at the top, bottom, or sides of the CRF.
15. Do not type data onto CRFs.
16. Do not obscure, mark over, or punch holes through the barcode at the top of each CRF.
17. Never use correction fluid (“white-out”) or correction tape on CRFs.
18. The site staff member who initially completes the CRF **must** record his/her initials **and** the date in the space provided in the bottom right-hand corner of each CRF page.
19. Remove any paper clips, staples, or other attachments before transmitting CRFs.

13.3.2 Marking 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.

Correct:



Incorrect:



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

13.3.3 Recording 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:

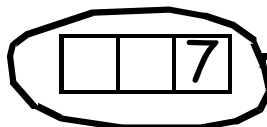
1. Right justify all numbers and fill in any blank leading boxes with zeroes. If boxes are left blank, a QC note will be applied asking for the boxes to be filled in.

The following example shows how a value of 7 is recorded in three response boxes:

Correct:



Incorrect:



→ This example would result in a QC note.

2. Write the number as large as possible while staying within 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:



Incorrect:



3. Write the number 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

13.3.4 Recording 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* in order for the date to be read in DataFax. Abbreviations for the months in English are shown below (Table 13-2).

Table 13-2: Month Abbreviations

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

For example, July 26, 2011 would be recorded as follows:

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

Sometimes, only a month and a year are required (for example, a 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 2002 would be recorded as follows:

O	C	T	0	2
<i>MMM</i>			<i>yy</i>	

13.3.5 Recording Time

Time is recorded on DataFax CRFs using the 24-hour clock in which hours are designated from 0–23. For example, using 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>	

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
12:00 a.m. (mid-night)	00:00*		12:00 p.m. (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
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

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

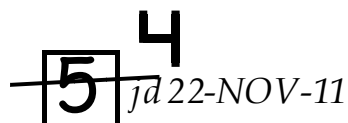
13.3.6 Data Corrections and Additions

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 transmission. It is important to make these changes to the original CRF—**never copy data onto a new form and never write over an entry once it is recorded**. After making the change, the CRF must be retransmitted to SCHARP DataFax. If a correction or addition is made to one page of a multiple-page CRF, only retransmit the page that was changed.

Whenever an entry on a DataFax CRF is changed, clarified, or amended, 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.

Correct:

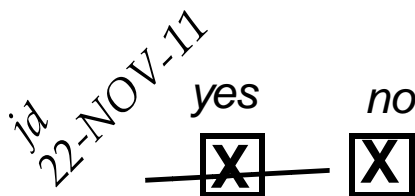


Incorrect:



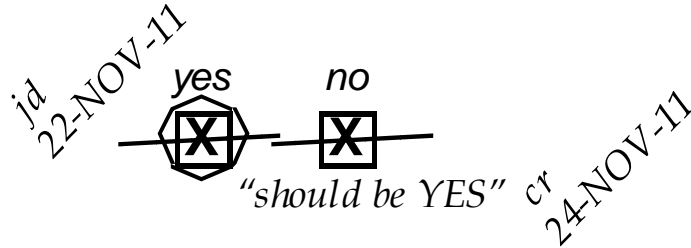
If an **X** is marked in the wrong response box, correct it by doing the following:

- draw a single horizontal line through the incorrectly marked box (do not obscure the entry or make it un-readable with multiple cross-outs),
- mark the correct box, and
- initial and date the correction and 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.



Please note that it is helpful to write in the final answer (e.g. “should be yes”) on the CRF when multiple corrections to one item have been made.

If an *entire* CRF needs to be deleted from the database, do the following:

- draw a single diagonal line across the entire page that needs to be deleted and write “delete”.
- include a brief note of explanation, and initial and date the deletion.

The standards above must 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. After making the change, the CRF must be retransmitted to SCHARP DataFax.

If a correction or addition is made to one page of a multiple-page CRF, only re-transmit the page that was changed.

13.3.7 Correcting a Participant Identification Number (PTID) Error

If the wrong PTID is submitted to SCHARP, in addition to making the correction on the original CRF, the Data Coordinator must be notified by email immediately. A PTID is a “key field”, meaning it is used by DataFax to identify where data is saved in the database. Therefore, simply correcting a PTID on a CRF creates a duplicate record: saving one CRF under two different PTIDs. The Data Coordinator must combine both CRFs under the correct PTID. Additionally, if the PTID used incorrectly is a valid PTID, belonging to a different participant, erroneous QCs may fire on that participant’s QC report until the incorrect CRF is deleted.

13.3.8 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, in addition to initialing and dating the entry.

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:

ym
15-OCT-11
don't know

 	 	A	P	R	0	0
<i>dd</i>		<i>MMM</i>			<i>yy</i>	

If an answer is no longer unknown, line through any previously lined-through boxes (using a diagonal line) and update the form with the new response, as shown below:

ym
~~15-OCT-11~~
~~*don't know*~~

 	 	A	P	R	0	0
<i>dd</i>		<i>MMM</i>			<i>yy</i>	

should be 15 ym 22-OCT-11

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.

13.3.9 Rounding Lab Values

- When recording a lab value on a case report form, it may be necessary to round the result up or down, as appropriate, to the level of precision allowed on the CRF.

Example: Lab reported hemoglobin value = 11.06 g/dL

If the following appears on the CRF...

		.		<i>g/dL</i>
--	--	---	--	-------------

...round the lab-reported value up to the tenths place and record as:

1	1	.	1	<i>g/dL</i>
---	---	---	---	-------------

- If the lab value is reported in a unit other than that which appears on the CRF (and therefore needs to be converted to the units that appear on the CRF), first perform the conversion, then round the converted results. Do not round on interim steps when performing the conversion.

Example: Lab reported creatinine value = 128 $\mu\text{mol/L}$

If the following appears on the CRF:

--	--

 .

--

mg/dL

First, convert from $\mu\text{mol/L}$ to mg/dL using the conversion factor (88.4). $128 \div 88.4 = 1.4479638$.

Then, round the converted value down to the tenths place and record as:

0	1
---	---

 .

4

g/dL

13.4 Site Review of Case Report Forms

Each form must be reviewed for completeness and legibility, ideally twice: once before the participant leaves the site and once again, by a second reviewer, before being transmitted to SCHARP DataFax. As part of these reviews, the site should check to ensure that:

- Other than the PTID, there is **no** information on the form that could uniquely identify the participant (e.g., no name, phone number, national identification number, or any other personal identifiers)
- A response has been recorded for each item, unless the item has been skipped as instructed by a skip pattern, or the item has been marked as unknown/refused
- All text responses are clearly recorded
- There are no marks on or above the DataFax barcode at the top of each CRF page.
- There are no
 - missing dates,
 - missing visit codes,
 - incorrect PTIDs,
 - incorrect visit codes,
 - missing data for items beginning a series of skip patterns,
 - inconsistent or discrepant data

Reviewers can make edits/updates to forms completed by another staff member, so long as they mark their corrections with their own initials and the date of the change. While CRFs are being reviewed, it is important that they are stored and tracked systematically. Sites should thoroughly describe their CRF review process (including who performs the review and how it is conducted) as well as timeframes for review in their Data Management SOP.

13.5 Faxing CRFs to SCHARP DataFax

To streamline the submission of DataFax forms, the site should identify which staff member(s) will be responsible for transmitting forms to SCHARP DataFax and which staff member(s) will be responsible for receiving and responding to QC reports.

Forms should be transmitted as soon as possible after they have been completed and reviewed. **Ideally, completed forms will be transmitted to SCHARP within 1-2 days of a participant completing the visit**, though up to 5 days is allowed. Additionally, sites should respond promptly to requests for clarifications and corrections included in the QC Reports. Early detection of CRF-related issues provides an opportunity to reduce errors and improve data quality.

It is necessary to have a system to identify whether a CRF has been transmitted to SCHARP DataFax. Such a system may include using a stamp to date the back of the CRF. If a date stamp is used, it is important to remember to use *only* the back of the CRF for a date stamp, *never* the front, and to date stamp the back of the CRF each time it is transmitted, including retransmissions.

13.5.1 CRF Tracking System (CTS2)

Sites can also confirm the receipt of faxed CRFs at SCHARP by using the CRF Tracking System (CTS2). If a site chooses to sign up to use CTS, they must send the CRFs to SCHARP in batches (groups) of multiple pages and track these batches. Two reports will be e-mailed to the site: the CRF Reception Report, indicating how many pages were received at SCHARP, and the CRF Validation Report, indicating which CRFs were received. If any discrepancies between the batches sent and SCHARP's report are found, it is then the site's responsibility to check the batches for the specific CRFs that were not received. The site determines how often to receive these e-mails (e.g., every day or several times a week). To sign up for CTS, contact the SCHARP Project Manager to receive a registration form.

Specific data transmission procedures, including timeframes, case report form storage locations before and after faxing, and mechanisms for identifying when forms have been transmitted, should be documented in the site's MTN-016 Data Management SOP.

13.6 Study Visit Information

13.6.1 Women Study Visits

Screening and Enrollment Visit

The Screening and Enrollment Visit is defined as Day 0 for the woman participant. This is the day she provides written informed consent to be screened and enrolled into the study. For MTN-016, a woman participant is considered enrolled once the participant has met all eligibility criteria and provided informed consent.

Quarterly Visits

While the woman is still pregnant, she will follow a quarterly visit follow-up schedule. The number of follow-up visits for this study will vary per participant, as it will depend upon how far along in the pregnancy she is. The greatest number of possible quarterly visits is 3 based on the maximum gestational period. See Table 13-3 for details regarding the target dates and visit windows for each Quarterly Visit.

Pregnancy Outcome

In cases when the woman enrolls into MTN-016 *prior* to the pregnancy outcome, the Pregnancy Outcome CRF will be part of a regularly scheduled Quarterly Visit or Interim Visit (see Interim Visits section below), and will be approximately when the outcome of the pregnancy becomes known to study staff. All procedures of the Quarterly Visit must be completed if the Pregnancy Outcome Visit occurs within the Quarterly Visit window, plus completion of the Pregnancy Outcome form.

In cases when the woman enrolls into MTN-016 *after* the pregnancy outcome, the Pregnancy Outcome Visit will be completed on the same day as the Screening and Enrollment Visit. In these cases, Quarterly Visits will not be completed. Note: MTN-016 allows for a woman to enroll in the study within one year after her pregnancy outcome.

The Pregnancy Outcome Visit does not signify termination from the study, but does signify the end of follow-up until a subsequent pregnancy is reported or a valid reason for termination occurs.

Pregnancy Cycles

As stated in the MTN-016 Protocol, Section 5.1, “participants and their infants can be enrolled for subsequent pregnancies; subsequent pregnancies of an EMBRACE participant will require a separate informed consent process to be initiated.” For a given woman participant, each pregnancy that meets the eligibility criteria for MTN-016 is referred to as a cycle. Each subsequent pregnancy may happen at any time after the initial pregnancy is completed. Please see Table 13-5 for the required CRFs to be completed at the beginning of each pregnancy cycle. In addition, see section 13.2.8 for information on pregnancy numbers (a way to document each pregnancy cycle).

Termination

Since mothers can enroll multiple pregnancies into the study, they should stay enrolled in MTN-016 until they have completed follow-up in the parent study. As stated above, the Pregnancy Outcome Visit does not signify the end of study participant, just the end of follow-up for a given pregnancy.

Once it has been determined that the mother will no longer be participating in MTN-016 (most likely because she has been terminated from the parent protocol), she should be terminated from MTN-016. There is no special Study Exit Visit for MTN-016; however, sites do need to document the termination by completing the Woman

Termination CRF. Sites also need to update the Concomitant Medications Log and re-fax it to SCHARP DataFax (see section 13.7, the Schedule of Forms).

13.6.2 Infants Study Visits

Newborn/Initial Visit

When possible, this visit should occur during the first ten days of life. The infant date of birth is defined as Day 0 for the infant participant. For MTN-016, an infant participant is considered enrolled if the infant 1) is born alive, 2) was consented into the study, and 3) attended at least 1 study visit.

Months 1, 6, and 12 Visits

There are 3 scheduled follow-up visits for the infants in MTN-016; Month 1, 6, and 12. There is no formal Termination or Study Exit Visit for infants in MTN-016. Therefore, study exit procedures will be part of the Month 12 Visit procedures. See Table 13-4 for details regarding the target dates and visit windows for each follow-up visit.

13.7 Target Days, Visit Windows, Split Visits & Missed Visits

13.7.1 Target Dates

Target dates are the days in which visits should *ideally occur*. Target dates are based on the date of enrollment for mothers and on the date of birth for infants. For *women*, the visits are targeted to occur quarterly (Day 90, Day 180 and Day 270) throughout the pregnancy following the participant's enrollment into the study (Day 0). For *infants*, the visits are targeted to occur at Month 1 (Day 30), Month 6 (Day 182) and Month 12 (Day 364) following the participant's date of birth (Day 0). Target dates do not change, even if a visit takes place before or after the target date.

13.7.2 Visit Windows

Visit windows include the days in which visits are *allowed to occur*. The visit window for the *women participants'* follow-up visits is 45 days before or after the target date (i.e. +/- 45 days). See Table 13-3. For example, if a woman participant enrolls into MTN-016 on 15 November 2013, her first Quarterly Visit target date is 14 February 2014. However, she can complete her Quarterly Visit #1 any time between 31 December 2013 and 30 March 2014.

Table 13-3: MTN-016 Target Visit Dates and Visit Windows: WOMEN

All visit windows are in days; Enrollment date = Day 0

Visit	Visit Code	Day Visit Window Opens	Target Date	Day Visit Window Closes
Enrollment	1.0	N/A	0	N/A
Quarterly #1	2.0	46	90	135
Quarterly #2	3.0	136	180	225
Quarterly #3	4.0	226	270	315

The visit windows for the *infant participants*’ follow-up visits are as follows: the Newborn Visit must be completed within 10 days after the infant’s date of birth; the Month 1 Visit has a 2 week window before or after the target date (i.e. +/- 2 weeks); and the Month 6 and Month 12 Visits have a 30 day window before or after the target date (i.e. +/- 30 days). See Table 13-4. For example, if an enrolled infant participant was born on 22 February 2014, the Month 1 target date is 24 March 2013. However, the Month 1 Visit can be completed any time between 10 March 2014 and 07 April 2014.

Table 13-4: MTN-016 Target Visit Dates and Visit Windows: INFANTS

All visit windows are in days; Date of birth = Day 0

Visit	Visit Code	Day Visit Window Opens	Target Date	Day Visit Window Closes
Newborn	1.0	0	0	10
Month 1	2.0	16	30	44
Month 6	3.0	152	182	212
Month 12	4.0	334	364	394

Visits completed within the visit window will appear on the MTN-016 Retention Reports as being completed “on-time”. Visits that are not completed within the visit window will be considered “missed” and relevant CRFs should be completed to document the missed visit (see section 13.7.4 for more information on Missed Visits).

SCHARP will provide sites with a Visit Scheduling tool (an Excel spreadsheet) that may be used to generate individual participant follow-up visit calendars. The spreadsheet requires that the participant’s enrollment date (for women participants) or date of birth (for infant participants) be entered. Once the enrollment date/birthdate is entered, the target date and visit windows for the follow-up visits will appear in the spreadsheet, which can then be printed and added to the participant’s study notebook. The women participant calendar tool provides potential visit scheduling for up to 4 pregnancy cycles for each woman. The tool can be found on the MTN web portal.

13.7.3 Split Visits

In cases where a participant is not able to complete all required visit evaluations on the same day, the participant may come back and complete the remaining evaluations on another day, as long as the evaluations are completed within the visit window for that particular visit (see Tables 13-3 and 13-4). For example, an infant comes for her Month 6 Visit on the target date and completes all required evaluations. However, the site suspects the infant has a major malformation but is unable to photograph the infant at this visit. The infant can return within the Month 6 visit window to complete the photographs.

13.7.3.1 Visit Codes for Split Visits

When a split visit occurs, the case report forms completed for the visit are all assigned the same visit code (even though some forms and evaluations will have different visit

dates). For example, an infant participant comes in for the Month 6 Visit on the target date of 23 January 2014 and completes all required evaluations except for the infant physical exam (the mother did not have time to stay at the clinic for all procedures to be completed). The infant returns on 25 January 2014 and completes the physical exam. All case report forms completed on 23 and 25 January are assigned a visit code of 3.0 (since all evaluations are Month 6 evaluations).

13.7.4 Missed Visits

In those cases where a participant is not able to complete any part of a required visit within the visit window, the visit is considered missed. For example, if a mother who enrolls into MTN-016 on 10 February 2014 (visit window for Quarterly Visit #1 = 28MAR14 – 25JUN14) shows up for her first Quarterly Visit on 29 June 2014, her Quarterly Visit #1 is considered missed, as she is now in the visit window for her second Quarterly Visit (26JUN14 – 23SEP14). Missed visits must be documented by completing a Missed Visit CRF (i.e. Woman Missed Visit CRF or Infant Missed Visit CRF).

If an infant is enrolled into MTN-016 after the window for the Newborn/Initial Visit (or any other subsequent visit) has passed, all visits that would have been completed but were missed need to be documented in DataFax with an Infant Missed Visit CRF. For example, if an infant enrolls into MTN-016 when she is 6 months old, an Infant Missed Visit CRF would need to be completed for the Newborn/Initial Visit as well as the Month 1 Visit.

If a visit happens to be completed within the visit window after a Missed Visit form has already been submitted to SCHARP, draw a diagonal line through the previously submitted Missed Visit form, include a brief note of explanation, initial and date the changes, and re-submit the form to SCHARP DataFax. Complete all of the scheduled visit procedures, code all forms with the scheduled visit code, and transmit the CRF pages.

Remember: Missed visits are considered protocol deviations in MTN-016. A Protocol Deviation Log does not need to be completed, however. Instead sites need to record the corrective action plan in the comments section of the Woman Missed Visit CRF or the Infant Missed Visit CRF for all missed visits that count as protocol deviations.

13.7.5 Interim Visits

In addition to the scheduled, protocol-required visits, Interim Visits may occur after enrollment into the trial. A clinic visit is considered an Interim Visit when a participant comes to the clinic for reasons *other* than to complete regularly scheduled (required) study visit procedures.

Interim visits may be performed at any time during the study for reasons that are administrative (a participant has study-related questions for the staff), lab-related (a par-

participant needs a lab test repeated for confirmation), or clinical (a participant needs additional clinical follow-up), for example. Phone contact with a participant is also considered an Interim Visit if the phone contact results in reporting a pregnancy outcome or new social harm. Given the specification of visit windows for this study, interim visits will occur when more than one visit takes place within a visit window. The following are examples of interim visits for MTN-016:

1. A mother enrolled in MTN-016 completes all required evaluations for the scheduled study visit within the target window. The participant then returns to the site clinic within the same visit window to report a pregnancy outcome.
2. A mother enrolled in MTN-016 completes all required evaluations, including an ultrasound exam, for the scheduled study visit within the visit window. The participant then returns to the site clinic within the same visit window for a repeat follow-up ultrasound exam.

If DataFax CRFs are required to document the visit (or phone call), an Interim Visit CRF must be completed and faxed to SCHARP DataFax. If no CRFs are required for the interim visit (for example, the participant comes to the clinic to obtain more condoms), the interim visit may be documented by a chart note only; it does not need to be assigned an interim visit code.

13.7.5.1 Visit codes for interim visits

Interim visit codes are assigned using the following guidelines:

- In the box to the left of the decimal point, record the one-digit visit code for the most recent scheduled visit (whether that visit was completed or missed).
- Use the guide below to complete the box to the right of the decimal point:
 - #.1 = the first interim visit after the most recent scheduled visit,
 - #.2 = the second interim visit after the most recent scheduled visit,
 - #.3 = the third interim visit after the most recent scheduled visit, and so on.

Example: A woman participant returns to the site clinic two weeks after completing her first Quarterly Visit to report a pregnancy outcome. If she is still in the Quarterly #1 Visit window, this current visit is considered an interim visit and is assigned the following interim visit:

Visit Code for this Interim Visit:

Visit Code **2**.**1**

13.7.6 Early Termination

A participant may voluntarily withdraw from the study at any time. Site investigators may also withdraw participants from the study (see Protocol Section 9.1). If the participant is willing and able, she will be asked (or the infant will be asked) to complete

one final study visit before terminating early. Specific procedures for early termination visits are included in SSP Section 6.

13.7 MTN-016 Schedule of Forms

The SCHARP-provided case report 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 tables (Table 13-5 and Table 13-6) list the DataFax and non-DataFax forms that are **required** to be completed at each MTN-016 study visit for Women and Infants.

Table 13-5: Case Report Form Completion Schedule: WOMEN

SCREENING AND ENROLLMENT		PREGNANCY # / VISIT CODE: 1 / 1.0
Form Acronym	Form Name	Plate #
<i>Required</i>		
GSH-1–GSH-5	Genetic Screening History	101–105
PPP-1	Parent Protocol Participation*	080
PR-1	Pregnancy Report and History	440
CM-1	Woman Concomitant Medications Log	423
DEM-1	Woman Demographics*	001
WEN-1	Woman Enrollment	070
UR-1	Ultrasound Results	120
<i>Non-DataFax</i>	Woman Medical History Log	N/A
*These CRFs are only completed once, even if a woman enrolls a new pregnancy.		
<i>As Needed</i>		
PO-1–PO-3	Pregnancy Outcome	441–443
QUARTERLY VISITS		PREGNANCY # / VISIT CODES: 1 / 2.0, 3.0, 4.0
Form Acronym	Form Name	Plate #
<i>Required</i>		
UR-1	Ultrasound Results	120
WFU-1	Woman Follow-up Visit	125
<i>As Needed</i>		
GSH-1–GSH-5	Genetic Screening History†	101–105
PO-1–PO-3	Pregnancy Outcome	441–443
SHA-1	Social Harms Assessment Log	155
CM-1	Woman Concomitant Medications Log†	423
<i>Non-DataFax</i>	Woman Medical History Log†	N/A
†Update and refax these forms, if applicable (refax DataFax forms only), at each Quarterly Visit.		

NEW PREGNANCY CYCLE		
SUBSEQUENT ENROLLMENT PREGNANCY # / VISIT CODE: 2 (3, 4, ETC.) / 1.0		
Form Acronym	Form Name	Plate #
<i>Required</i>		
GSH-1–GSH-5	Genetic Screening History	101–105
PR-1	Pregnancy Report and History	440
UR-1	Ultrasound Results	120
CM-1	Woman Concomitant Medications Log**	423
WSC-1	Woman Subsequent Consent	075
<i>Non-DataFax</i>	Woman Medical History Log (<i>updated</i>)	N/A
<i>As Needed</i>		
PO-1–PO-3	Pregnancy Outcome	441–443
** If a woman enrolls a new pregnancy, the previously completed Concomitant Medications Log(s) just needs to be updated and faxed again.		
QUARTERLY VISITS PREGNANCY # / VISIT CODE: 2 (3, 4, ETC.) / 2.0, 3.0, 4.0		
Form Acronym	Form Name	Plate #
<i>Required</i>		
UR-1	Ultrasound Results	120
WFU-1	Woman Follow-up Visit	125
<i>As Needed</i>		
GSH-1–GSH-5	Genetic Screening History†	101–105
PO-1–PO-3	Pregnancy Outcome	441–443
SHA-1	Social Harms Assessment Log	155
CM-1	Woman Concomitant Medications Log†β	423
<i>Non-DataFax</i>	Woman Medical History Log†	N/A
†Update and refax these forms, if applicable (refax DataFax forms only), at each Quarterly Visit. β At the mother’s final study visit, the Woman Concomitant Medications Log must be updated and re-faxed.		
TERMINATION/STUDY EXIT		NO VISIT CODE
<i>Required</i>		
TM-1	Woman Termination	490

Table 13-6: Case Report Form Completion Schedule: INFANTS

NEWBORN/INITIAL VISIT* (SEE BELOW)		VISIT CODE:
1.0		
Form Acronym	Form Name	Plate #
Required		
CM-1	Infant Concomitant Medications Log	423
IEN-1	Infant Enrollment* (see below)	070
IPE-1	Infant Physical Exam	130
IFV-1	Infant Visit	125
<i>Non-DataFax</i>	Infant Medical History Log	N/A
As Needed		
HTR-1	Infant HIV Test Results	136
IVL-1	Infant Vaccination Log	301
<i>Non-DataFax</i>	LDMS Specimen Tracking Sheet	N/A
MONTH 1 VISIT		VISIT CODE: 2.0
Form Acronym	Form Name	Plate #
Required		
IPE-1	Infant Physical Exam	130
IFV-1	Infant Visit	125
As Needed		
CM-1	Infant Concomitant Medications Log†	423
HTR-1	Infant HIV Test Results	136
IVL-1	Infant Vaccination Log†	301
SHA-1	Social Harms Assessment Log	155
<i>Non-DataFax</i>	Infant Medical History Log†	N/A
<i>Non-DataFax</i>	LDMS Specimen Tracking Sheet	N/A
†Update and refax these forms, if applicable (refax DataFax forms only).		
MONTH 6 VISIT		VISIT CODE: 3.0
Form Acronym	Form Name	Plate #
Required		
IPE-1	Infant Physical Exam	130
IFV-1	Infant Visit	125
As Needed		
CM-1	Infant Concomitant Medications Log†	423
HTR-1	Infant HIV Test Results	136
IVL-1	Infant Vaccination Log†	301
SHA-1	Social Harms Assessment Log	155
<i>Non-DataFax</i>	Infant Medical History Log†	N/A
<i>Non-DataFax</i>	LDMS Specimen Tracking Sheet	N/A
†Update and refax these forms, if applicable (refax DataFax forms only).		

MONTH 12 VISIT		VISIT CODE: 4.0
Form Acronym	Form Name	Plate #
<i>Required</i>		
CM-1	Infant Concomitant Medications Log ^β	423
IPE-1	Infant Physical Exam	130
TM-1	Infant Termination	490
IFV-1	Infant Visit	125
<i>Non-DataFax</i>	Infant Medical History Log (<i>updated</i>)	N/A
<i>As Needed</i>		
HTR-1	Infant HIV Test Results	136
IVL-1	Infant Vaccination Log	304
SHA-1	Social Harms Assessment Log	155
<i>Non-DataFax</i>	LDMS Specimen Tracking Sheet	N/A
^β At an infant's final study visit, the Concomitant Medications Log must be updated and re-faxed.		

*If the Newborn/Initial Visit is missed, the Infant Enrollment form must still be completed whenever the infant is enrolled into the study. Since an infant can complete an enrollment visit at any time point between birth and age 1 (12 months), a Missed Visit CRF must be faxed in for all infant visits that are missed prior to enrollment. If an infant presents for screening and enrollment during a period that falls outside of one of the infant visit windows, the screening and enrollment procedures may be conducted as part of an interim visit. At this interim enrollment visit, sites would fax in all forms normally completed at a Newborn/Initial Visit, including the Infant Enrollment form, as well as the Infant Interim Visit CRF.

13.9 How to Complete 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. Below are interviewing techniques that may be useful.

13.9.1 Interviewing Techniques

An interviewer uses both verbal and non-verbal techniques (if the interview is being conducted in person and not over the telephone) to obtain the most honest, accurate, and thorough responses from participants.

Some techniques to remember include:

- Make the participant feel welcome
- Be comfortable with the questions you are asking
- Always remain neutral
- Speak slowly and clearly
- Probe a participant if he/she is having a hard time coming up with an answer

These techniques are discussed below.

Welcoming the Participant

- When a new participant arrives at the clinic, everything about the study is new. Help make the participant feel comfortable.
- Perhaps offer the participant a glass of water or other beverage.
- Introduce yourself, and try to create rapport (connection) between yourself and the participant to help her feel comfortable during the interview.
- Some DataFax forms include introduction statements before certain items to help prepare the participant for sensitive questions. Read each of these introductions as they appear on the forms.

Asking Sensitive Questions

Your level of comfort with asking sensitive questions will affect the participant's comfort and answers. If you ask the questions in a confident and supportive manner, the participant will feel more confident and comfortable answering the questions. Make eye contact with the participant to let her know that you are listening to her and aware that she is being asked difficult questions. Avoid apologizing for questions or making facial gestures that might show you feel any way but neutral about a question or the participant's response. If the participant feels judged for her behavior, she will be less likely to share honestly with you.

Pacing the Interview

Every participant is different. Some will know or say the answer to questions very quickly. Others may have to think longer to come up with answers, or may change their answers after giving more thought to the subject. Always account for this variety when doing an interview. Read items slowly. Let the participant finish thinking before you record her response and go on to the next item.

Reading Items Aloud

For MTN-016 we have not translated the interviewer-administered forms as they are more clinical in nature. You must review each item on the relevant CRFs with the participant. If an item is not understood, provide explanation or interpretation, if necessary. Avoid tangential—though related—counseling and educational discussions during data collection. When applicable, acknowledge questions and concerns raised by the participant during the interview, and state that the subject can be discussed after the end of the interview.

Vary your tone of voice, so that you don't sound automated. Emphasize the important words in an item, so that the meaning of the question comes through.

When given the option, choose “clinical” versus “street” or “vernacular” language based on participant preferences/cues.

For items with multiple sub-items, review all sub-items with the participant and mark the appropriate response for each, based on participant report.

Probing

One of the major goals of the study's interviews is to obtain accurate genetic history for each woman enrolled. These interviews ask participants to recall many aspects of their family medical history. However, participants may not remember or know the answer to every question. The technique for helping a participant remember an answer, clarify a response, decide between two similar but different answers, or report something more precisely is called "probing."

Effective probing helps a participant think more about a question or refine an answer that is too general; however, probing must not bias or otherwise direct participant responses. As the interviewer, you cannot offer the participant an answer. Therefore, all probes must be neutral.

The following are some probing strategies to use when a participant initially answers "don't know" to an item, or cannot refine his/her response enough to allow for adequate documentation.

- **Repeat Probe:** The repeat probe is used by repeating the item or response categories (if the response categories are part of the question). Although the participant might hear you the first time you ask a question, he/she may need to hear the question more than once to provide an answer. Instead of rephrasing a question if you notice the participant is confused, first repeat the item as it is written. Sometimes hearing the question a second time is all that is needed.
- **Echo Probe:** The echo probe involves repeating the participant's exact response. Sometimes hearing the answer with a different voice will help the participant respond more precisely. Always repeat the participant's response in a neutral, non-judgmental way.
- **Silent Probe:** The silent probe is used by pausing briefly after a participant gives what seems to be an uncertain answer. Although silence can feel awkward, sometimes it is helpful when a participant is trying to determine the most accurate answer to a question. Use a silent probe when the participant sounds unsure of his/her answer and may need some extra time to think more carefully about the question.
- **Non-verbal Probe:** The non-verbal probe is used by giving hand or facial gestures that may help the participant to come up with an answer. Remember that all such gestures must be neutral and nonjudgmental.
- **Specification Probe:** The specification probe is used by asking the participant to give a more precise answer. Although a participant may give an answer that he/she considers accurate, it may not be specific enough for purposes of form completion. For example, an item asks for the exact number of times the participant did something and he/she answers with a range ("5 to 10"). In this case, the probe, "Can you be more specific?" is often enough to help the participant give the most accurate response.

- **Historical Probe:** The historical probe is used by asking whether the event in question occurred any time around major holidays or personal events such as a birthday or other life event. Some items require the participant to recall dates, and initially he/she may be unable to recall a specific date. Referencing a calendar can also help the participant remember dates.

13.9.2 Watching for Non-verbal Cues

A participant may give you one answer verbally, but express something else using body language or facial expressions. Although you should not question a participant so as to make her feel like you don't trust her answers, be aware of whether she is giving you non-verbal cues that indicate she is not feeling comfortable, not taking the interview seriously, or not answering honestly.

13.9.3 Checking Your Work

During the interview it is important to use the forms instructions (those on the front and back of each page) to guide the interview. Also, make sure the participant is understanding and responding to you, and record all reported information on the forms. **After the interview and while the participant is still there**, review the forms for accuracy and completeness so you can complete an item that might have accidentally been missed.

13.10 Additional Form Completion Instructions

Detailed form completion instructions for each form are provided on the back of each form page. These instructions include the purpose of each form as well as how each form should be completed. 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 some additional instructions for the several case report forms. In addition, form instructions that were included in Data Communiques are also added here.

13.10.1 Infant Concomitant Medication Log (CM-1)

- All concomitant medications taken throughout the course of the study, starting from screening, should be recorded on the CM-1.
- Each time a new entry is added or an existing entry is modified on the CM-1, the form page should be faxed to SCHARP DataFax. Do not wait to complete all entries on a page before faxing it to SCHARP DataFax.
- (*From Data Communiqué #3, 13AUG13*): The instructions on the Infant Concomitant Medications Log have been updated to include a reminder that vaccinations can no longer be recorded on the CM-1; all infant vaccinations should now be recorded on the Infant Vaccination Log.

13.10.2 Infant Developmental Screening CRF (IDS-1)

- (From Data Communique #4, 01MAY14): The developmental screening assessment has been eliminated from MTN-016 protocol version 2.0. This form should no longer be administered at the Month 6 Visit or the Month 12 Visit.
- However, please reference **MTN Operational Guidance 2**, which was distributed on 17MAR14. This Operational Guidance states that, “If MTN-008 sites submit protocol version 2.0 to their regulatory bodies and receive approval, they should continue to conduct the developmental screening assessment for any infants enrolled in the study under protocol version 1.0. This includes completing the Infant Developmental Screening form at the appropriate visits.” So, for infants enrolled under version 1.0 of the protocol whose parent protocol is MTN-008, the Infant Developmental Screening form will still need to be completed at the Month 6 and Month 12 visits.

13.10.3 Infant Enrollment (IEN-1)

- (From Data Communique #5, 14SEP15): Evaluation of gestational age using the Ballard pediatric assessment has been eliminated from MTN-016 protocol version 2.0. Therefore, item 4 on the IEN-1 should be marked as “not assessed” for all infants enrolled into MTN-016.

13.10.4 Infant HIV Test Results (HTR-1)

- (From Data Communique #4, 01MAY14): Items 2b and 3b on the HTR have been updated to include revised lower limits of detection that better match current viral load platforms.
- In addition, items 2a and 3a have been revised to allow for viral load results of “target not detected” as well as “detected, under the limit of detection”.
- **Viral Copies/mL Reported:** When the lab result is a number, record the number exactly as it appears on the report. Select the appropriate operator in item 2a or 3a and record the exact number in the adjacent boxes.

Example of Local Lab Result from the Abbott M2000 Assay

<u>Copies / mL:</u> 4,914,478	<u>Log Base 10 Value</u> 6.69
Run comment:	
Sample comment:	
Reportable Range:	The Abbott RealTime HIV-1 RNA assay range of quantitation is 40 to 10,000,000 copies/mL.

Example of Completed HTR-1 using the Abbott M2000 Assay Results

Not done/ Not collected <input type="checkbox"/>	Alternate Collection Date		
	<i>dd</i>	<i>MMM</i>	<i>yy</i>
	2 4	A P R	1 4
2. HIV RNA			
2a. HIV RNA PCR (plasma)	> <input type="checkbox"/>	= <input checked="" type="checkbox"/>	< <input type="checkbox"/>
	viral copies/mL		
	0 4 9 1 4 4 7 8		
	OR <input type="checkbox"/>		
	detected, under the limit of detection		
	OR <input type="checkbox"/>		
	target not detected		
2b. HIV RNA PCR kit lower limit of detection	20 <input type="checkbox"/>	40 <input checked="" type="checkbox"/>	OR <input type="checkbox"/>
	viral copies/mL		
	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		

- Target Detected:** When the lab result says “<20, RNA target detected” or “<40, RNA target detected” but the reportable range further explains that “viral RNA was detected *but is below the lower limit of quantification*”, mark “detected, under limit of detection” in item 2a or 3a.

Example of Local Lab Result from the Roche TaqMan Assay

Copies / mL:	Log Base10 Value
<20, HIV-1 RNA target detected.	<1.30
Run comment:	
Sample comment:	
Reportable Range:	The COBAS TaqMan HIV-1, version 2.0 Test assay range of quantitation is 20 to 10,000,000 copies/mL. The result reported indicates viral RNA was detected but is below the lower limit of quantitation of the COBAS TaqMan HIV-1, version 2.0 Test assay.

Example of Completed HTR-1 using the Roche TaqMan Assay Results

Not done/ Not collected <input type="checkbox"/>	Alternate Collection Date		
	<i>dd</i>	<i>MMM</i>	<i>yy</i>
	2 4	A P R	1 4
2. HIV RNA			
2a. HIV RNA PCR (plasma)	> <input type="checkbox"/>	= <input type="checkbox"/>	< <input type="checkbox"/>
	viral copies/mL		
	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
	OR <input checked="" type="checkbox"/>		
	detected, under the limit of detection		
	OR <input type="checkbox"/>		
	target not detected		
2b. HIV RNA PCR kit lower limit of detection	20 <input checked="" type="checkbox"/>	40 <input type="checkbox"/>	OR <input type="checkbox"/>
	viral copies/mL		
	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		

Example of Local Lab Result from the Abbott M2000 Assay

Copies / mL: <40, HIV-1 RNA target detected.	Log Base 10 Value <1.60
Run comment:	
Sample comment:	
Reportable Range: The Abbott RealTime HIV-1 RNA assay range of quantitation is 40 to 10,000,000 copies/mL. The result reported indicates viral RNA was detected but is below the lower limit of quantitation of the Abbott RealTime HIV-1 RNA assay.	

Example of Completed HTR-1 using the Abbott M2000 Assay Results

Not done/ Not collected <input type="checkbox"/>	Alternate Collection Date		
	<i>dd</i>	<i>MMM</i>	<i>yy</i>
2. HIV RNA	<input type="text" value="2"/> <input type="text" value="4"/>	<input type="text" value="A"/> <input type="text" value="P"/> <input type="text" value="R"/>	<input type="text" value="1"/> <input type="text" value="4"/>
2a. HIV RNA PCR (plasma)	> <input type="checkbox"/> = <input type="checkbox"/> < <input type="checkbox"/>	<i>viral copies/mL</i>	OR <input checked="" type="checkbox"/> <i>detected, under the limit of detection</i> OR <input type="checkbox"/> <i>target not detected</i>
2b. HIV RNA PCR kit lower limit of detection	20 <input type="checkbox"/> 40 <input checked="" type="checkbox"/>	<i>viral copies/mL</i>	OR <input type="text" value=""/> <input type="text" value=""/> <input type="text" value=""/>

- Target NOT Detected:** When the lab result says “target not detected” and there is no further explanation in the reportable range, mark “target not detected” in item 2a.

Example of Local Lab Result from the Abbott M2000 Assay

Copies / mL: <40, HIV-1 RNA target not detected.	Log Base 10 Value No log calculated
Run comment:	
Sample comment:	
Reportable Range: The Abbott RealTime HIV-1 RNA assay range of quantitation is 40 to 10,000,000 copies/mL.	

Example of Completed HTR-1 Using the Abbott M2000 Assay Results

Not done/ Not collected <input type="checkbox"/>	2. HIV RNA	Alternate Collection Date										
		dd	MMM	yy								
		2	4	A	P	R	1	4				
	2a. HIV RNA PCR (plasma)	>	=	<	viral copies/mL				OR	detected, under the limit of detection	OR	target not detected
		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>								<input checked="" type="checkbox"/>
	2b. HIV RNA PCR kit lower limit of detection	20	40	viral copies/mL								
		<input type="checkbox"/>	<input checked="" type="checkbox"/>	OR								

- For more information about viral load testing, refer to MTN-016 Laboratory SSP Section 12.

13.10.5 Infant Missed Visit CRF (MV-1)

- (From Data Communique #4, 01MAY14): The instructions on the back of the Infant Missed Visit form have been updated to provide clarification that sites should record a corrective action plan for a missed visit protocol deviation in the comments section of the Infant Missed Visit CRF.

13.10.6 Infant Physical Exam CRF (IPH-1)

- (From Data Communique #2, 22FEB13): Items 18 and 18a have been added to document any nutritional concerns which may be observed during the infant physical exam and whether the infant is referred for clinical follow-up. In order to make room for these new items, please note that some previous items have been merged (e.g. head/neck/scalp).

13.10.7 Infant Protocol Deviation Log (PDL-1)

- (From Data Communique #4, 01MAY14): This form documents all MTN-016-related protocol deviations for infants. The completed form should be faxed to SCHARP DataFax in the same manner as all the other CRFs completed for this study. This form is not included in the Schedule of Forms. However, it can be sent it at any point in time during the study.
- Missed Visits are counted as protocol deviations in MTN-016. However, the PDL does not need to be completed in an infant misses a visit. We will know that a protocol deviation due to a missed visit has occurred by the presence of the Infant Missed Visit CRF. Since sites are required to record a corrective action plan for a protocol deviation, sites should record this information in the comments section of the Infant Missed Visit CRF.
- Not all missed infant visits in MTN-016 count as protocol deviations. An infant can enroll into the study at any time point up until s/he is 1 year old (12 months). For DataFax reasons, sites are required to complete an Infant Missed Visit form (MV-1) for all infants that are enrolled after the Newborn/Initial Visit – one MV-1 for every study visit the infant has missed prior to enrollment. For example, if

the infant enrolls at the Month 6 Visit, the site would complete an MV-1 for the Newborn/Initial Visit and as well as an MV-1 for the Month 1 Visit. In this scenario, the missed visits that occurred before the infant was enrolled will NOT count as protocol deviations, and sites do not need to record a correction action plan on the MV-1.

13.10.8 Infant Safety Event Log (ISL-1)

- (From Data Communiqué #4, 01MAY14): The ISL is no longer required to be used in MTN-016.

13.10.9 Infant Vaccination Log (IVL-1)

- (From Data Communiqué #3, 13AUG13): A new Infant Vaccination Log was created so that sites can document all vaccinations administered to infants using vaccination codes (included below). Vaccinations administered to infants must no longer be recorded on the Infant Concomitant Medications Log.

INFANT VACCINATION LOG CODES	
Vaccine	Code
Bacille Calmette-Guerin (BCG)	01
Diphtheria, Pertussis, and Tetanus (DPT)	02
Diphtheria, Tetanus, and Acellular Pertussis (DTaP)	03
Diphtheria, Tetanus, Acellular Pertussis and Haemophilus Influenzae Type B (DTaP-Hib)	04
Diphtheria, Tetanus, Acellular Pertussis, Inactivated Polio, and Hepatitis B (DTaP-IPV-HepB)	05
Diphtheria, Tetanus, Acellular Pertussis, Inactivated Polio, and Haemophilus Influenzae Type B (DTaP-IPV-Hib)	06
Hepatitis A (HepA)	07
Hepatitis B (HepB)	08
Haemophilus Influenza Type B (Hib)	09
Haemophilus Influenzae Type B and Hepatitis B (Hib-HepB)	10
Haemophilus Influenzae Type B, Hepatitis B, and Inactivated Polio (Hib-HepB-IPV)	11
Influenza (IIV, LAIV, INF)	12

Inactivated Poliovirus (IPV)	13
Measles (ME)	14
Measles, Mumps, Rubella (MMR)	15
Oral Poliovirus (OPV)	16
Pneumococcal Conjugate (PCV)	17
Rotavirus (RV)	18
Varicella (VAR)	19
Other vaccination	99

13.10.10 Infant Visit CRF (IFV-1)

- *(From Data Communiqué #2, 22FEB13):* Sites will no longer document the growth percentiles on the Infant Visit CRF. Instead these must be recorded on the WHO growth charts (published by the Centers for Disease Control and Prevention, 1 November 2009, and found on the MTN-016 website) for each infant at each visit.

13.10.11 Pregnancy Outcome CRF (PO-1)

- *(From Data Communiqué #1, 07APR11):* There is a skip rule from item 5 if one of the first two response options is marked. If the pregnancy outcome is a “full – term live birth” or a “premature live birth”, item 6 should not be completed.

13.10.12 Ultrasound Results CRF (UR-1)

- *(From Data Communiqué #1, 07APR11):* The Ultrasound Results form must be completed at all required visits (i.e. Enrollment and all Quarterly Visits). If ultrasound exam results are not available at a particular required visit, mark the “no” response box for item 1. You must also mark a reason for item 1a. If results are not available, record the date of the required visit for the Exam Date in the upper right hand corner. For example, if the first Quarterly Visit occurs on 23JUN14, and there are no ultrasound results available at this visit, you will record “23JUN14” as the exam date and mark item 1 “no” and mark the appropriate reason for item 1a.

13.10.13 Woman Concomitant Medication Log (CM-1)

- All concomitant medications taken throughout the course of the study, starting from screening, should be recorded on the CM-1.

- Each time a new entry is added or an existing entry is modified on the CM-1, the form page should be faxed to SCHARP DataFax. Do not wait to complete all entries on a page before faxing it to SCHARP DataFax.

13.10.14 Woman Missed Visit CRF (MV-1)

- (*From Data Communique #4, 01MAY14*): The instructions on the back of the Woman Missed Visit form have been updated to provide clarification that sites should record a corrective action plan for a missed visit protocol deviation in the comments section of the Woman Missed Visit CRF.

13.10.15 Woman Protocol Deviation Log (PDL-1)

- (*From Data Communique #4, 01MAY14*): This form documents all MTN-016-related protocol deviations for mothers. The completed form should be faxed to SCHARP DataFax in the same manner as all the other CRFs completed for this study. This form is not included in the Schedule of Forms. However, it can be sent it at any point in time during the study.
- Missed Visits are counted as protocol deviations in MTN-016. However, a Woman Protocol Deviation Log does not need to be completed if a woman misses a visit. We will know that a protocol deviation due to a missed visit has occurred by the presence of the Woman Missed Visit CRF. Since sites are required to record a corrective action plan for a protocol deviation, sites should record this information in the comments section of the Woman Missed Visit CRF.

13.10.16 Parent Protocol Participation (PPP-1), Woman Follow-up Visit (WFU-1), Woman Interim Visit (IV-1)

- (*From Data Communique #6, 16MAY17*): Item 2a on the Parent Protocol Participation CRF, item 2a on the Woman Follow-up Visit CRF, and item 3a on the Woman Interim Visit CRF ask you to record the visit code of a parent protocol visit if the participant completed an MTN-016 visit at the same time as a parent protocol visit. If the visit code from the parent protocol contains two digits to the right of the decimal point, and the first digit to the right of the decimal point is a “0”, remove the first 0 after the decimal point before recording it onto the MTN-016 CRF. For example, if recording a parent protocol visit code of “3.02” onto item 2a of the Parent Protocol Participation CRF, remove the 0 after the decimal point and record “3.2” onto item 2a. If the parent protocol visit code that you need to record onto the MTN-016 CRF is higher than 3.09 (e.g. 3.10), contact the SDMC Clinical Data Manager for more information.

13.11 Miscellaneous Information

13.11.1 Specimen Label Supply

- SCHARP will ensure sites have access to specimen labels (printed on-site). Specimen labels should be used for all primary specimen collection containers.

Please refer to the Laboratory section of the SSP (Section 12) for more information on laboratory specimen collection and labeling.

13.12 Case Report Forms

All MTN-016 case report forms developed for the study are posted on the MTN-016 Atlas page in the “CRFs” section:

<https://atlas.scharp.org/cpas/project/MTN/016/begin.view?>

Detailed form completion instructions for each form are provided on the back of each form page. Refer to the Visit Checklist of a given visit for a suggested order in which the forms should be completed at that visit.