
MTN-003 Data Communiqué #1

September 9, 2009

This communiqué is official study documentation for MTN-003. It is considered part of the MTN-003 Study-Specific Procedures (SSP) Manual. Please circulate this communiqué among relevant staff for their review, and print and file a copy in Section 15 of each MTN-003 SSP Manual maintained at your site.

UPDATES

1. Screening Part 2 Medical Eligibility Form (non-DataFax) – Updated Page 3, Dated 31-AUG-09

On 31-AUG-09, SCHARP updated page 3 of the non-DataFax Screening Part 2 Medical Eligibility form. The previous version was missing the “yes” and “no” response boxes for item 51. SCHARP has corrected this, and the response boxes are now present on the updated version of the form page. SCHARP will include the updated page in all future form shipments to MTN-003 sites. In addition, SCHARP has replaced the previous version of the form page with the updated version in Section 14 of the SSP Manual, which is available on the MTN-003 web page. The version number and version date for Section 14 remain the same, but the updated version date of the form page is shown in the footer of that page.

2. Participant-reported Baseline Medical and Menstrual History Form (non-DataFax) – Updated Page 5, Dated 02-SEP-09

On 02-SEP-09, SCHARP updated page 5 of the non-DataFax Participant-reported Baseline Medical and Menstrual History form. The previous version contains three items which are not required because the information requested in these items is collected on page 6 of the same form. The three items are:

- Menstrual symptoms worse than her usual menstrual symptoms
- Vaginal bleeding or spotting between her usual menstrual periods
- Post-coital bleeding

To eliminate duplication, SCHARP has removed these three symptoms from page 5 of the form. Participants’ usual menstrual symptoms should be recorded in the item “Usual menstrual symptoms” on page 6 of the form. Vaginal bleeding or spotting between menstrual periods, including post-coital bleeding, should be recorded in the item “Usual non-menstrual genital bleeding pattern” on page 6 of the form. SCHARP will include the updated page in all future form shipments to MTN-003 sites. In addition, SCHARP has replaced the previous version of the form page with the updated version in Section 14 of the SSP Manual, which is available on the MTN-003 web page. The version number and version date for Section 14 remain the same, but the updated version date of the form page is shown in the footer of that page.

CLARIFICATIONS

1. Documenting Genital Bleeding

All cases of participant-reported genital bleeding occurring between usual menstrual periods will be documented on baseline and follow-up medical and menstrual history source documents. For sites using the SCHARP-provided non-DataFax medical and menstrual history forms, this information will be recorded on page 6 of the Participant-reported Baseline Medical and Menstrual History form and page 3 of the Participant-reported Follow-up Medical and Menstrual History form. The non-DataFax Pelvic Exam Diagrams form is used to record all pelvic exam findings, both normal and abnormal. This means that all clinically observed genital blood/bleeding, whether expected, unexpected, menstrual, or non-menstrual, should be documented on the Pelvic Exam Diagrams form. In contrast, the Screening and Enrollment Pelvic Exam form and Follow-up Pelvic Exam form are used to record *only* abnormal pelvic exam findings. Genital bleeding is only considered an abnormal finding if it is unexpected. This means that only clinically observed menstrual or non-menstrual bleeding that is unexpected should be recorded on these forms.

Expected non-menstrual bleeding should not be considered abnormal and therefore, during follow-up, should not be documented as an adverse event (AE). Expected non-menstrual bleeding may include a small amount of cervical bleeding that can occur with speculum insertion or specimen collection, provided the bleeding is not associated with a tissue finding (e.g., abrasion) and the Investigator of Record (IoR) or designee deems the amount of bleeding to be within the range of normal. If cervical blood/bleeding observed with speculum insertion or specimen collection exceeds that which is expected, in the opinion of the IoR or designee, the cervical blood/bleeding should be considered abnormal, documented as “cervical friability,” and graded according to the “Cervical edema and friability” row of the DAIDS Female Genital Grading Table.

If it is unclear whether a genital bleeding event (during follow-up) is expected or unexpected, complete the non-DataFax Genital Bleeding Assessment form.

2. Documenting Vaginal pH and Wet Mount Results on the Vaginal Test Results Form

Per protocol, each time a pelvic exam is done, vaginal pH must be assessed and the results must be recorded in item 1b on the Vaginal Test Results form. Vaginal pH must be recorded regardless of whether wet mount testing for vaginal candidiasis, vaginal trichomoniasis, or bacterial vaginosis (BV) is performed.

Wet mount testing for vaginal candidiasis should be performed when clinically indicated. When wet mount testing is clinically indicated, the result should be recorded in item 1f of the Vaginal Test Results form; otherwise, item 1f should be marked “not done.”

Wet mount testing for vaginal trichomoniasis is not expected to be performed in MTN-003. When testing for trichomoniasis is required per protocol or clinically indicated, the trichomonas rapid test should be performed, with the result recorded in item 2 of the Vaginal Test Results form. In the rare event that wet mount testing for trichomoniasis is performed, the result should be recorded in item 1e of the Vaginal Test Results form; otherwise, item 1e should be marked “not done.”

Wet mount testing for BV is not expected to be performed in MTN-003. When testing for BV is clinically indicated, the BV rapid test should be performed, with the result recorded in item 3 of the Vaginal Test Results form. In the rare event that wet mount testing for BV is performed, the results should be recorded in items 1a, 1c, and 1d of the Vaginal Test Results form; otherwise, items 1a, 1c, and 1d should be marked “not done.”

3. Recording Conditions on the Medical and Menstrual History Source Documents

The Participant-reported Baseline Medical and Menstrual History form and the Participant-reported Follow-up Medical and Menstrual History form may not provide enough space to adequately document participant-reported medical conditions. If more space is needed, all information required to adequately document a reported condition should be recorded in chart notes (or on another designated site-specific source document). In such cases, record “see chart notes” next to the condition on the Participant-reported Baseline Medical and Menstrual History form or the Participant-reported Follow-up Medical and Menstrual History form.

4. Defining Sexual Assault for the Baseline Medical and Menstrual History Assessment

History of sexual assault must be assessed as part of the baseline medical and menstrual history performed at Screening Part 2. For purposes of this assessment, sexual assault is defined as:

Forced sexual contact that usually involves force upon a person without consent, or is inflicted upon a person who is incapable of giving informed consent (due to age, physical or mental capacity). This includes forced sexual contact with a husband or partner, a family member, friend, stranger, or other person.

The clinician performing the assessment should keep this definition in mind when asking the participant probing questions to identify and document any history of sexual assault. For example, the clinician may ask, “Has anyone ever forced you to have sexual contact with him or her when you did not want to? This could include vaginal, oral, or anal sex forced upon you by your husband or partner, a family member, friend, stranger, or other person?”

5. Completing Item 22 on the Screening Part 1 Eligibility Form (non-DataFax)

Item 22 of the non-DataFax Screening Part 1 Eligibility form requires the interviewer to transcribe the participant’s response from item 12 on the same form. However, it is possible that item 12 will be left blank, per the skip pattern, if the response to item 11 is “no” or “don’t know”. In these cases, please line through the item 22 response boxes, write “not applicable” next to the boxes, and initial and date the note.

6. Recording the Date and Time of Last Dose on the Specimen Storage/PK (SS) Form

Items 6-8 on the Specimen Storage/PK form capture the date and time of the participant’s last dose of study product prior to the visit. Per protocol, collection of these data is required at quarterly, semiannual, annual, and product use end visits, to coincide with specimen collection for testing of study drug levels (blood PK analyses). For the other study visits in which the Specimen Storage/PK form is completed, mark the “N/A” box for items 6-8.

7. Measuring and Documenting Participant Weight on the Safety Laboratory Results Form

Per protocol, participant weight should be measured and documented at the Screening Part 1, Screening Part 2, Month 1, quarterly, semiannual, annual, and product use end visits. In addition, weight should be measured whenever blood is collected for serum creatinine testing and when clinically indicated. For visits in which serum creatinine is tested, site staff should transcribe participant weight in item 3d of the Safety Laboratory Results form. If serum creatinine is not tested at a given visit, participant weight does not need to be recorded on the Safety Laboratory Results form; in this case, mark the “Not done/Not Collected” box for item 3d.

REMINDERS

1. Grading Lab Values According to the DAIDS Toxicity Table

Depending on a site’s local laboratory reference ranges, it is possible that a participant can have a laboratory value that falls within the site’s normal range, but is still gradable (severity grade 1 or higher) per the DAIDS Toxicity Table. Always refer to the DAIDS Toxicity Table to determine whether or not a lab value is gradable. For gradable lab values that occur during follow-up, refer to the participant’s baseline value for the given test to determine whether or not there is an increase in severity that warrants documentation of a new AE.

2. Completing the Safety Laboratory Results (SL) Form for Gradable Lab Values

If a lab value is gradable (severity grade 1 or higher) per the DAIDS Toxicity Table, always record the severity grade in the “Severity Grade” box, regardless of whether the specimen was collected at screening, enrollment, or follow-up. Record the “AE Log Page #” if the gradable lab value is reportable as a stand-alone AE (e.g., “proteinuria”) or is part of a reportable clinical AE (e.g., “urinary tract infection”). If a gradable lab value does not meet criteria for AE reporting (i.e., the specimen was collected before enrollment/randomization, or the severity grade represents an ongoing pre-existing condition), mark the “Not Reportable as an AE” box. If a severity grade is recorded in the “Severity Grade” box, either an “AE Log Page #” must be recorded, or the “Not reportable as an AE” box must be marked. The same “AE Log Page #” may be recorded for the same item on SL forms completed at consecutive visits, for example, if a lab value AE persists at the same or lesser severity across study visits.

SCHARP has added this clarification to page 14-25 of Section 14 of the SSP Manual, which is available on the MTN-003 web page. The version date for this page has been updated to 04-SEP-09.

3. Documenting and Reporting AEs of Gradable Lab Values

When documenting gradable lab values as AEs - and determining the term to assign to the AEs - site staff should consider whether or not the participant received (or was offered) treatment for the condition. If the participant did receive (or was offered) treatment for the condition, document the AE with a term that includes a clinical diagnosis. For example, if a participant has a gradable decreased phosphate value and receives treatment for it, site staff should document the AE as “hypophosphatemia” (rather than “decreased phosphate”). For purposes of AE reporting, treatment is not limited to the prescribing of medications. In this example, treatment may include a clinician’s recommendation that the participant supplement her diet with phosphate-rich foods. If the participant did not receive (or was not offered) treatment for the gradable lab value, site staff should document the AE with the direction of abnormality (increased or decreased). In this example, site staff would document the AE as “decreased phosphate.”

The “Date Reported to Site” on the AE Log form should be the date that site clinic staff first become aware of the gradable lab value. For safety labs, this will be the date the lab result report is received at the site clinic. The “Onset Date” recorded in source documents and in item 2 of the AE Log form should be the date of specimen collection. The visit code recorded in item 10 of the AE Log form should be the visit code assigned to the specimen collection date; this should be the same visit code that is assigned to the AE “Onset Date”. The “Status/Outcome Date” (item 6a) should be the collection date of the follow-up specimen that yields one of the following: 1) a non-gradable result, 2) a return to baseline severity (if the AE represents the worsening of a pre-existing condition), or 3) a result of increased severity (thus requiring documentation of a new AE).

SCHARP has added this clarification to page 14-26 of Section 14 of the SSP Manual, which is available on the MTN-003 web page. The version date of this page has been updated to 04-SEP-09.

4. Recording Recruitment Codes for Item 18 on the Demographics (DEM) Form

Each site is responsible for developing and maintaining a site-specific list of codes that represent the various sources from which women are referred or recruited for screening in VOICE. These sources may include local health clinics, hospitals, community locations, non-study medical and psychosocial providers, and referrals from other participants (via word-of-mouth). Codes may also be assigned to various versions of recruitment flyers, posters, etc. For each participant who screens in VOICE, record in item 18 on the DEM form the recruitment code that represents the source from which the participant was referred or recruited. Once accrual is underway at a given site, the site is encouraged to request a breakdown of this data on a periodic basis from SCHARP to help guide future recruitment strategies.