
MTN 001 Data Communiqué #3

November 7, 2008

This is official study documentation for MTN 001. Please circulate it among relevant staff for their review, print it, and place it in your MTN 001 SSP Manual in the Data Communiqués section. This document is considered part of the MTN 001 SSP manual.

UPDATES

None

CLARIFICATIONS

1. Documenting Contraceptive/Family Planning Methods During Study Follow-up

Sites should assess any changes in participants' family planning methods at each study follow-up visit, and should document this information in the participant chart notes. The documentation should include start dates for any new family planning method reported, and stop dates for any family planning method reported as discontinued. Documentation should also include any reported non-adherence to a given family planning method. If the participant reports no changes since her last study visit, record this in the participant chart notes to document that family planning methods were assessed at the given visit.

The participant chart notes are considered source for family planning data during study follow-up, and should be used as source to complete the Family Planning Methods case report form.

2. Documenting Menstrual History During Study Follow-up

Sites should assess any changes in participants' menstrual cycles at each study follow-up visit, and should document this information in the participant chart notes. Documentation should include the start and stop dates of the participant's last menstrual period, as well as any changes in flow or number of days between menses. Documentation should also include any changes in type and severity of menstrual symptoms. If applicable, report any adverse events (AEs) on the AE Log case report form and grade according to the DAIDS Female Genital Grading Table for Use in Microbicide Studies. (Refer to SSP Manual Section 10.5 for further information on clinical management and documentation of genital bleeding events). If the participant reports no changes since her last study visit, record this in the participant chart notes to document that menstrual history was assessed at the given visit. If the participant is amenorrheic, document the amenorrhea in the participant chart notes. If the amenorrhea is unexpected, also document the associated severity grade (per the DAIDS Female Genital Grading Table for Use in Microbicide Studies), if applicable.

The participant chart notes are considered source for menstrual history data during study follow-up. The chart notes (and not the non-DataFax Follow-up Medical History Log) should be used as source when completing items 1 and 2 on the non-DataFax Genital Bleeding Assessment case report form.

3. Measuring and Documenting Participant Weight

The determination of creatinine clearance by the Cockcroft-Gault equation is required at each regularly scheduled study visit through Week 21, and at interim visits if clinically indicated. The equation requires participant weight. Thus, sites must weigh study participants at each regularly scheduled study visit in order to calculate creatinine

clearance for that visit. Due to weighing scale variability, it is important that the same scales be used at each visit, and that sites calibrate their scales on a weekly basis. In addition, site staff should make sure that study participants are wearing indoor clothing without shoes or other heavy items of clothing when they are weighed. These measures will help ensure that changes in creatinine clearance over time are not due to variability in weight measurement.

Participant weight should be documented on the non-DataFax Physical Exam form completed for a given visit. It is transcribed onto the Pharmacokinetics-Intensive or Pharmacokinetics-Non-intensive form at each mid- and end-of-study period visit, since participant weight is also required for the pharmacokinetics (PK) analysis.

4. Protocol Requirements for Intensive Pharmacokinetic (PK) Specimen Collection Times

At the end-of-study period visits, collection of blood and genital specimens must occur, per protocol, between 30 minutes before and 30 minutes after the assigned sample time AND within 30 minutes of each other. For example, a participant comes to the clinic for her Week 6 Visit. She was randomized to a sampling time of 2 hours post-dose, and takes her observed dose of study product at 9:30 AM. The site should aim to collect her 2-hour post-dose blood and genital specimens at 11:30 AM. At minimum, these specimens should be collected no earlier than 11:00 AM and no later than 12:00 PM. If the blood is collected at 11:40 AM, the genital specimens must be collected between 11:10 AM and 12:00 PM.

For the Week 13 and Week 20 Visits, these specimens must also be collected within 15 minutes of the same time point in which they were collected at Week 6. In the example above, the participant had her 2-hour post-dose blood specimen collected at 11:40 AM, which was 2 hours and 10 minutes after the dosing time. At her Week 13 and Week 20 Visits, site staff should aim to collect her 2-hour post-dose blood specimens 2 hours and 10 minutes after dosing as well.

The protocol allows for intensive PK specimens to be collected within defined ranges of time, as noted in the above examples. However, for purposes of analysis, it is important that sites make effort to collect PK specimens as close to the assigned sampling time as possible.

5. Documenting Anal Study Gel Insertion for Participants in the Oral Study Period

Item 8 on the Study Product Adherence and Behavior Assessment (version dated 24-OCT-08) asks about anal insertion of study gel, and is asked at all mid- and end-of-study period visits. When this question was developed and added to the form, the consensus of the protocol team was to ask this question of all study participants in all study periods. The rationale is that, while participants in the oral study period are not dispensed study gel, use of study gel (including anal use) is still possible in the oral period. For example, there could be sharing of study gel among participants, and use of study gel dispensed during a previous study period (vaginal and/or dual). Since anal insertion of study gel will affect the PK measures, this question is asked at all study periods to maximize the chances of capturing all reported insertions of study gel anally.

Item 8 may cause more confusion when asked at the Week 3 and Week 6 Visits of participants randomized to the oral period first. (In total 24 of the 144 participants slated to enroll in the study will be randomized to the oral period first). For these participants, it is recommended that site interviewers provide participants with further explanation if a participant is in the oral study period and does not understand the question. For example, as follow-up the interviewer can ask the participant if she had any study gel in her possession during the 3-week period in question. If she responds “no”, then the interviewer can clarify with the participant that she did not in fact insert study gel anally, and mark “no” for item 8.

REMINDERS

None