MTN-003D Operational Guidance: IDI Probing on Blood Tests

DATE: 7 January 2013

TO: MTN-003D Technical Team

FROM: Miriam Hartmann on behalf of the MTN-003D Operations Team

CC: MTN-003D Protocol Team

Dear MTN-003D Technical Team,

The purpose of this memo is to provide guidance related to a new area for probing during the IDI guide administration. The primary new area of interest relates to the following topic:

- Perceptions of what participant's own drug levels in blood will be during blood tests.

See the question by question (QxQ) guide below for suggested incorporation of the above mentioned topic into the IDI guide (Q# 13). The new probe suggestion is included in ***bold italics*** and highlighted in gray. Previously added probe suggestions from the operational guidance issued on 13 December 2012 are included in ***bold italics.*** It is recommended that this guidance be reviewed by all interviewers prior to their next scheduled interview and available during IDI administration. Interviewers may discard their copies of the 13 December 2012 operational guidance and replace with this guidance.

Question/Probes	Intention & Probing Suggestions
1. Can you tell me all the reasons that you joined VOICE? • How did the benefits you received for participating in VOICE influence your decision? (e.g. reimbursements, getting health checked regularly, etc.) • How did your personal life influence your decision? (e.g. partners/husband, family members, employment status, etc.) • How did your community/the place where you live influence your decision? (e.g. community opinions/feelings about research in general and the study in particular)	• Explore the reasons that the participant joined the VOICE trial, including factors such as the trial benefits, aspects of her personal life, and aspects of her community that contributed to the decision. • ***If the participant is unable to respond to the current wording of question/probes, consider asking "What would you say to a friend who was thinking of joining a trial like VOICE about the reasons for joining such a trial?"***
2. Before you joined VOICE, how worried were you about getting HIV or having HIV? • What made you feel that way? • How did these feelings influence your joining VOICE?	• Review how the participant perceived her risk for HIV **before** joining the study, what contributed to her self-perception of risk, and whether this influenced her joining the study.
3. During VOICE, how worried were you about	• Explore participant's perception of HIV risk

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getting or having HIV? • How did these feelings influence whether you used or didn't use the VOICE [tablets/gel]? • How did these feelings or worries about getting HIV change over time during your VOICE participation? What made them change? (e.g. regular HIV tests, use of the product, change in risk behaviors, etc.)	**during** the study, how these feelings influenced use of the study product ***(including timing of product use)***, and how these worries/feelings changed over time and why. • Discussion of reasons for change may touch on study procedures or factors from the participant's life.
Before we talk about the [tablets/gel], I'd like to get a better idea of the things that were going on in your life during your VOICE participation. 4. Thinking about the time between when you first joined VOICE and when you ended the study, did anything big change in your life? (e.g. changed partners, school/studies/jobs, got married, got pregnant, moved households, death of a significant other, etc.) Tell me about what changed. • When did it change? *[Note to interviewer: use the timeline tool to help the participant estimate when the change occurred. We're mainly interested in whether the participant was still using the product for any period of time after the change.]* • How did this affect your product use?	• Discuss any major changes in the participant's life that occurred while she was in the VOICE study. • If there has been change, explore when they broadly occurred in relation to the study (e.g. towards the beginning, middle, or around PUEV) and how they affected adherence to the study product.
Now I'd like to talk more about factors that may have influenced women's ability and willingness to use the [tablets/gel] in the VOICE trial. We know [taking a tablet/using a gel] every day is hard to do and a lot of people in VOICE weren't able to use the [tablets/gel] every single day. That's okay. What we'd like to understand better is what made it hard for some people to use the [tablets/gel]. 5. What were the reasons it was difficult for <u>VOICE women</u> in general to use the [tablets/gel] every day for the whole duration of VOICE?	• Explore reasons for non-adherence among VOICE participants in general. • Explore reasons that made it difficult to use the products on a daily basis, at different points of the trial (e.g. beginning, middle, end), and what might have made it difficult to use products for the full duration of the trial (e.g. long trial period, interim DSMB results, etc.).
6. Think about what life is like for women here in [Harare/Kampala/Durban]. Please describe the aspects about this place or this society that might have made it difficult for women to use [tablets/gel] every day during VOICE? (e.g. local leaders, church groups, societal attitudes towards research, etc.) • How did those aspects make it harder <u>for you</u>?	• Investigate how the socio-cultural context may have negatively affected women's adherence to the study product, as well as how this context influenced the MTN-003D participant's adherence in particular. • Topics discussed may include community attitudes towards research in general or towards VOICE in particular, or issues around women's willingness and ability to autonomously use study products in

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	this context. • ***Explore the role of internalized or externally experienced stigma on product use.*** • ***If unable to use daily, probe on if product use timed with sexual activity.***
7. Now, think about the time you were participating in the VOICE study, are there aspects about VOICE or the study clinic that made it difficult for <u>you</u> to use the [tablets/gel] every day for the whole duration of VOICE? (e.g. clinic environment/location, visit schedule and length, relationship with staff in general, adherence counseling approach, interaction with counselors, etc.) • During the study, did you experience any change in how the staff counseled you on product adherence? How did this [change/lack of change] affect you and your product use? • What was helpful or not helpful about the product adherence counseling you received?	• Explore how aspects of the VOICE clinic, staff, or trial may have negatively impacted the participant's adherence. • Probe on VOICE counseling approach to determine if participant noticed the change from ASP to VASP and how this change affected her experience. • ***Probe on the influence of pharmacists and product return counts on product use, including the role of pharmacists in education/counseling and how their role may have changed during the study.*** • ***If nothing made it difficult, probe on what made it easier, what was liked best, or what made no difference.***
8. What were the [other] reasons it was difficult for <u>you</u> to use the [tablets/gel] every day for the whole duration of VOICE? (*Probe on major life changes mentioned above*) • Were there issues with your sexual partner(s) – main or others? • In your household or family? (e.g. crowding and privacy issues, family and marital responsibilities, etc.) • In your community? (e.g. neighbors, gossip, etc.)	• Establish other reasons, beyond those mentioned in questions 6-7, that made it difficult for the participant to use the study product consistently. • This may include factors related to their sexual relationships, within their household/family life, or in their community.
During your participation in VOICE you were asked many questions about product use. One question asked you to "rate in the past 4 weeks your ability to [take the tablets/use the gel] exactly as you were instructed." "Taking or using the product as you were instructed" is understood differently by different people. 9. What does that statement "[take the tablets/use the gel] exactly as you were instructed" mean to you? • How did you understand the question in terms of how often you were supposed to [take the	• Discuss how the participant understood the VOICE adherence rating question, especially as "taking the product exactly as you were instructed" may have been interpreted differently by each participant. • Probe about understanding in relation to various factors that she could have considered when responding to the question, such as frequency, timing, and ease/difficulty of using the product.

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tablets/use the gel]? • How did you understand the question in terms of the time of day you were supposed to use the product? • How did you understand the question in terms of how easy or difficult it was to use?	
Now let's talk about the different response options to this question – very poor, poor, fair, good, very good, and excellent. 10. What do each of these different response options mean to you? • If a woman answered "excellent", what do you think that meant? *[Note to Interviewer: use the show cards to have women discuss other response options that they view as different.]* • Is it possible that a woman could skip doses but still answer excellent or very good? Why/ why not? • If a woman used [the gel/both tablets] each and every day, would she have answered "excellent"? Why/ why not?	• Explore the participant's understanding of the rating scale response options and try to understand the different factors such as: o recall (e.g. how she remembered her behavior in the past 4 weeks), o numeracy (e.g. how she counted days), culture (e.g. modesty; wanting to please), or o other personal factors (e.g. low self-worth, emotional state) that may have contributed to women selecting certain responses.
11. What did you think about when you decided on your own response? • How much did you think about the response you selected before choosing it? • How much did you try to remember what you had actually done before responding? • What was your typical answer? Why did you choose that answer? • How did your response vary over time? Why did it vary?	• Discover the thought process behind the participant's answer to the adherence rating scale question, including: o what criteria she used to decide, o how she usually responded, how and o if it changed throughout the study.
Now, let's talk about other ways that product use was measured. In a different study, where women were asked to report on their everyday use of a gel or tablet, almost all women said that they used the product every day. But, when their blood was tested, only about half of the women who said that they used the product every day actually had the drug in their blood. 12. Why do you think there was a difference between what women said about their use of the product and what their blood tests showed? • If the women didn't actually use the products every day, what might have made them report that they did use it?	• Discuss inconsistences between self-reported adherence and study drug level in a previous trial (MTN-001) that used the same products as VOICE (tenofovir tablets and gel). • Explore the reasons that may have contributed to this discrepancy. • Probe on potential reasons women may have had for providing upwardly biased answers, including those related to study staff, clinic, or other factors. • ***Note that product return counts reflected self-reported adherence in this study and probe about potential discrepancies between product returns and actual use and what women did with their unused products***

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• Do you think there might have been anything about the study staff or the clinic that influenced their responses? • What other reasons would make women reluctant to report what was really going on with their use of the products?	
13. How do you think those study results compare to what may have happened with women in VOICE? • Was there anything about the VOICE clinics, the procedures or the staff that influenced women's ability to report times when the [tablets/gel] were/was not used? • How about for you?	• Find out whether the participant thinks that the same issues around the reporting discrepancy discussed in question 12, may have happened in VOICE and explore specific aspects of the trial, clinic, procedures, or staff might have made it difficult for women to report on their true adherence. • ***Probe about potential discrepancies between product returns and actual use in VOICE, and what women may have done with their unused products*** • Probe on whether the factors discussed impacted the participant's ability to accurately report **her own** adherence ***(i.e. her experience reporting high product use when actually she was not able to consistently use) or return products.*** • ***Expand on how the blood tests show levels of drug in the blood – and probe on how this would compare to the participant's self-reported adherence by asking: "Over the course of the VOICE trial, the VOICE staff tested your blood several times to determine if you used the [tablets/gel]. If we could look now at the results of those blood tests, what do you think the results would show?" Could use an example: "If you rated yourself as "very good" at a visit when your blood was tested, do you think the results of your blood test would show low, medium or high levels of drug in your blood?"***
14. What could the VOICE study have done differently to get more honest or accurate responses? • What could be changed about the clinics, procedures, or staff to make women feel comfortable reporting when they were not able to use the [tablets/gel]? • How could the counseling be changed to make women more comfortable in discussing their challenges with product use?	• Elicit suggestions for how the **VOICE study** could have made it easier for women to honestly report their adherence ***and return products***. • Probe on specific factors about the clinics, procedures, staff ***(including pharmacists)***, and adherence counseling.
In VOICE, you were asked about your use of the [tablets/gel] in a number of different ways (e.g. in	• Find out the best **manner or modality** (e.g. in person, on a computer, ***through product return***

Question/Probes	Intention & Probing Suggestions
interviewer administered questionnaires, ACASI, etc.). 15. How could questions about use of [tablets/gel] be asked to make women more comfortable reporting not using [tablets/gel]? • Does how the question is worded make a difference? How so?	***counts,*** or some other way) for asking questions on product adherence in order to elicit a more accurate response. • Probe specifically on how the wording of the questions could be improved to encourage honest and accurate responses.
16. What do you think is the best way staff should ask about use of [tablets/gel] to make participants most comfortable and get the most truthful answer? • Does it matter who asks the question? How so?	• Discuss how **study staff *(including pharmacists)*** could improve their way of asking adherence questions to encourage truthful answers. • Probe on how the role of the staff member affects a participant's ability to respond accurately (i.e. are they more free with certain types of staff rather than others).
17. Can you tell me what you heard about VOICE stopping the tenofovir tablets and gels early? • From whom did you hear about these results first? • Can you explain in your own words what you understand happened? • [*Probe about product not mentioned above:*] What about the [tablet/gel]?	• Discuss what the participant heard about the DSMB results that led to the stopping of the tenofovir tablets and the gel, who they heard it from, and how they understood what they heard.
18. [*For those who did not mention it above, explain that the tenofovir tablet and gel showed no protective effect against HIV in VOICE*] For what reasons do you think the tenofovir tablet and gel arms didn't show protection against HIV in VOICE? • What makes you think that? • What changed for <u>you</u> after you heard the results? (e.g. change in product use for those in Truvada arm; feelings related to being discontinued from the trial for those on the stopped arms, etc.)	• Find out why the participant thinks the tenofovir tablet and gel were not found to be protective against HIV. • Probe on how learning these results affected their feelings or behaviors related to the study, including continued product use (specifically for those in the Truvada/placebo tablet arms).
We've now reached the second part of our interview. During this part of our discussion, I'd like to talk about different sexual behaviors women may engage in. I'd like to start by using pictures to help us understand how you think about the female body. *[Note to Interviewer: Show the participant the visual template and probe around the following topics:* • *Identify different part of the ano-genital area such as vulva, urethra, vaginal opening and anus and discuss some of their functions(if appropriate)* • *Discuss ways one may feel pleasure or pain*	• Use the activity to determine the participant's understanding of their anus and genital areas, how they relate these areas to sexual pleasure/pain. • Also probe on the terminology used, specifically in relation to anal sex and sex from behind, and explore whether and how they understood the VOICE question on anal sex.

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• *Explore participant's words/terms for sexual behaviors, specifically vaginal sex from behind and anal sex* • *Ask how participant understood the VOICE ACASI question on anal sex: "In the past 3 months how many times have you had anal sex? By anal sex we mean when a man puts his penis inside your anus."* *After the exercise is finished, explain what is meant by anal sex in the context of the 003D study before moving on to the next section of the interview.]*	
Now let's talk a little more about anal sex. In the VOICE ACASI, women were asked how many times they had anal sex in the past 3 months. At the beginning of the VOICE study, almost 900 women said they had anal sex at least one time in the past 3 months. 19. How common do you think anal sex among women is in this area or community? • Is anal sex talked about openly? • Which types of people do you think have anal sex?	• Explore the community norms, attitudes and practice of anal sex in the participant's community, including types of women who engage in the practice.
20. What are all the reasons you think a woman might have anal sex?	• Examine what motivates women to have anal sex.
21. How do you think anal sex is generally introduced into a sexual relationship? • What types of relationships does it happen in? • Who suggests or initiates anal sex (the man, the woman, both)? Do women have a choice to say yes or no? • Does anal sex usually happen before or after a round of vaginal sex or does it happen when vaginal sex does not occur?	• Ask about how, in what types of relationships, and when within a relationship anal sex is first discussed or practiced. • Explore decision-making around anal sex. • Also probe on the timing of anal sex in relation to other sexual activities.
22. In what types of circumstances or situations do you think a woman might have anal sex? • Have you ever found yourself in a similar circumstance/situation? Can you tell me about it?	• Explore the types of context or scenarios in which a woman might have anal sex (e.g. with certain partners, during menses) and whether the participant has ever been in a similar scenario.
23. If a woman did have anal sex, what types of products would she use before or during sex? • Are there any cleansing practices that are common before people have anal sex? What are they? (e.g. enemas, douching)	• Discuss the products or practices associated with anal sex, such as cleansing practices, lubricants, condom use, or others.

Question/Probes	Intention & Probing Suggestions
• Would she use any type of lubricant during anal sex? Why or why not? • Would condoms be used? Why or why not? • What other type(s) of product would she use?	
Now let's think specifically about the women in VOICE who were using the gel. 24. Would a woman use the gel during anal sex? • Why or why not?	• Discuss the participant's views on whether VOICE gel arm women may have used the study product during anal sex and the reasons for this choice.
25. If she did use the gel, how would she use it? • Where would she use it? [*Use body mapping diagram if necessary*] • If she used the gel rectally, for what reasons would she put the gel in her anus? • [*If gel participant*] Have you ever found yourself in a situation when you used the gel rectally? Can you tell me about it?	• Understand how gel arm women may have used the gel during anal sex and the potential reasons for its use rectally. • If the participant was in the gel arm, explore her own experiences, if any, with using the gel rectally.
26. We have talked about a lot of different things today. Before we finish, I wonder if you have any questions for me or if you have any additional comments about your experience in VOICE or about the interview today?	• Allow for questions and comments about the interview and/or experience in VOICE.
27. Is there anything else that you think might have been important to the gel and tablet "failing" in VOICE, that we should think about or aspects of the VOICE study to improve upon for future trials?	• Offer an opportunity for further explanations as to why the tenofovir tablet/gel were not found to be effective and elicit additional suggestions related to how the study could improve future trials so as to avoid "failure."

Please note this is official study documentation and it should be filed as part of the study Essential Documents.