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**MICROBICIDE TRIALS NETWORK  
QUESTIONS AND ANSWERS**

**MTN-015:**

**An Observational Study of Women Who Acquired HIV While Participating  
in a Microbicide Trials Network Clinical Trial**

**1. What is the aim of MTN-015?**

MTN-015 is a long-term, observational study that seeks to understand the nature of HIV progression and treatment response in HIV-positive women who may have been using a topical microbicide or antiretroviral therapy as pre-exposure oral prophylaxis (PrEP) when they were infected. Researchers plan to follow women who acquire HIV while participating in a Microbicide Trials Network (MTN) trial, no matter what study group they had been assigned to in that trial.

**2. Why is this study important?**

MTN-015 is the first study to monitor women who become infected incidental to their participation in an HIV prevention trial of either a topical microbicide or oral PrEP. The study is essential for better understanding the impact of these agents on the natural history of HIV and for determining if the clinical course of HIV disease is made better or worse. Importantly, MTN-015 will help address theoretical questions about HIV drug resistance. Currently, very little is known about either the potential for or incidence of HIV drug resistance among those participating in trials of microbicides or PrEP. Information gained through this study will be critical to efforts focused on developing microbicide products and other HIV prevention approaches for high-risk populations.

**3. Who is conducting the study?**

MTN-015 is being conducted by a team of researchers working in the Microbicide Trials Network (MTN), a clinical trials network established in 2006 and funded by the National Institute of Allergy and Infectious Diseases (NIAID) and co-funded by the National Institute of Mental Health and the National Institute of Child Health and Human Development, all of the U.S. National Institutes of Health (NIH).

**4. Who is supporting the trial?**

MTN-015 is funded solely by the Division of AIDS, National Institute of Allergy and Infectious Diseases, part of NIH.

**5. What is a microbicide?**

Microbicides are substances that are designed to reduce or prevent the sexual transmission of HIV or other sexually transmitted infections (STIs) when applied topically to the vagina. A microbicide can be formulated in many ways, such as a gel or cream, or as a ring that would release the active ingredient over time. Some microbicides are also being developed for rectal use. Several microbicide products are being tested in clinical trials, including trials conducted by MTN, although none is yet approved or available for use by women.

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**6. What is pre-exposure prophylaxis (PrEP)?**

Pre-exposure prophylaxis, or PrEP, is an HIV prevention approach that typically involves the daily use of oral anti-retrovirals (ARVs) by people who are HIV negative. ARVs are drugs that are approved for treating HIV. A number of trials are underway that seek to determine if the approach is effective for preventing HIV as well. One trial being planned by MTN – the VOICE Study (Vaginal and Oral Interventions to Control the Epidemic) – will evaluate the effectiveness of both PrEP and vaginal microbicides for preventing sexual transmission of HIV in HIV-negative women.

**7. How is it possible that a woman could acquire HIV while taking part in a trial of a microbicide or PrEP, approaches meant to prevent HIV?**

To determine the safety and effectiveness of a particular candidate product or approach, researchers typically conduct the kind of trials that involve participants being randomly assigned to different treatment groups, including a “control” group that may use a placebo. Often, these trials are blinded, meaning neither researchers nor participants know who is in which treatment group. This is considered the best way to evaluate promising new approaches such as microbicides or PrEP, but it also means, however, that some participants will not receive the active gel or drug, and there is no guarantee that either approach will prove effective in those who do.

In addition, many of these trials are conducted in parts of the world where women are at very high risk for acquiring HIV through sexual intercourse. In order to reduce the risk of HIV for women participating in its trials, MTN researchers provide all trial participants free condoms, HIV testing and HIV risk-reduction counseling, including on the use of condoms, and routine testing and treatment for STIs. Despite these intensive, ongoing efforts, women participating in trials may still become infected with HIV.

**8. Can the microbicide or oral antiretroviral drug cause HIV in these women?**

As in all cases, only the virus can cause HIV infection. Therefore, neither the gels nor the oral antiretroviral drugs themselves cause HIV infection. In fact, the two antiretrovirals that are being evaluated in HIV prevention trials, including MTN’s VOICE Study, are drugs approved by regulatory authorities for the treatment of people with HIV.

**9. Where is MTN-015 being conducted?**

MTN-015 is open to women who are identified as becoming infected with HIV during participation in an MTN clinical trial. MTN trials are conducted at 17 clinical research sites in seven countries: Malawi, South Africa, Uganda, Zambia, Zimbabwe, India and the United States.

**10. How do women learn that they have been infected with HIV?**

Women in MTN clinical trials undergo frequent HIV testing throughout the course of the study. As such, some women may learn they acquired HIV during the course of their participation in the study. If at any time women test positive, study staff will provide counseling and refer her to services at local facilities that provide medical care and treatment, including antiretroviral therapy, and psychological and social support.

**11. How is the study designed?**

MTN-015 is an observational study in which researchers are following women who learned they became infected with HIV while participating in an MTN clinical trial to determine differences in HIV progression and response to antiretroviral therapy over time. Women who become infected during an MTN trial are counseled and referred by study staff to services at local facilities that provide medical care

and treatment for HIV infection, including ARV therapy, and psychological and social support. These services may be available within the same health care facility that houses the research site, with a program funded by the U.S. President's Emergency Plan for AIDS Relief through arrangements made by MTN site investigators or with another health care provider.

As part of the study, women make frequent visits to the research site for physical exams and laboratory tests that help researchers assess how the disease is progressing and how the women are responding to treatment. Specifically, researchers closely monitor the levels of HIV in the blood (HIV viral load), extent of damage to cells in the immune system (CD4+ T-cell count), virologic response to therapy and other health indicators to determine differences among women who had been using either an active microbicide or oral drug at the time of infection and women who had been assigned to a trial's placebo control group. Researchers plan to follow women until 2013, at which time the study period may be extended.

**12. Does the study include HIV treatment, including ARVs?**

MTN-015 does not provide HIV treatment, including ARVs, as part of the study. Women who participate in MTN-015 are referred for HIV treatment, medical management and psychological and social support at other local facilities where the level of care provided meets or exceeds the community standard for HIV care. However, with a participant's permission, MTN-015 researchers maintain close contact with her primary treatment provider and share results of laboratory tests that are performed as part of the MTN study, which may suggest modifications to her treatment and help improve the level of care.

**13. Do MTN-015 researchers know if women were using active products or placebos when they acquired HIV?**

No. Because most trials are blinded, neither women nor the researchers know who is in which study group or whether an active product or a placebo had been used at the time of infection. Some MTN trials may still be ongoing while participants are taking part in MTN-015. Therefore, study group information will remain blinded until the parent trial is completed and its data been analyzed and verified. Once the microbicide trial is completed, however, all participants are informed of their treatment assignment.

**14. What approvals were required for this trial to get underway?**

MTN-015 underwent extensive and rigorous review by NIAID, as well as by an institutional review board (IRB) or ethics committee (EC) at each trial site. Local IRBs and ECs ensure that studies are scientifically valid and ethically conducted and they provide oversight throughout the duration of a study or trial. In addition, each trial site has a local community advisory board to provide input on and oversight of study activities.

**15. Do women participating in the study provide informed consent?**

Written informed consent is obtained from each study participant prior to screening and enrollment using forms translated into local languages. The process ensures that women understand the procedures, as well as possible risks and benefits of the study. Participants are under no obligation to participate and may leave the study, without consequence, at any time.

**16. What are the medical benefits for women participating in the study?**

Study participants receive free laboratory tests and physical exams, counseling on preventing secondary HIV infection and free condoms. STI risk reduction counseling, testing and treatment is provided at no charge to both women and their partners. In addition, with a participant's permission, MTN-015 researchers can maintain close contact with her primary treatment provider and share results of laboratory tests that are performed as part of the study, which may suggest modifications to her treatment and help improve the level of care.

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**17. What is being done to ensure the safety of the participants?**

MTN-015 is an observational study, and therefore it involves no investigational products or procedures that are associated with significant risk to participants. While few safety concerns are expected as a result of study participation, site investigators closely monitor all study participants and report any unexpected concerns to the protocol team.

**18. Is there concern about the development of drug resistance?**

Some have raised the possibility that women who acquire HIV while using an ARV-based microbicide or ARV-based oral PrEP will fail to respond to future treatment consisting of the oral form of the drug or other drugs in the same class of ARVs, a process referred to as resistance. Others are concerned that becoming infected even years later could also confer drug resistance. Resistance occurs when a pathogen's sensitivity to a particular drug is diminished. With HIV, researchers believe drug resistance occurs as the virus mutates, each time incorporating a new disguise that renders itself unrecognizable as a drug target. Thus far, there has been no evidence of drug resistance in studies of tenofovir topical gel, including a Phase I study that involved both HIV-negative and HIV-positive women. While more extensive study is required, current research suggests resistance is less likely to occur with a vaginal microbicide than with an oral treatment. That's because microbicides are applied topically and the amount of drug that may be absorbed throughout the body is relatively small. However, there is no scientific or clinical information about the nature of resistance or the incidence of resistance among those using ARV-based microbicides or taking oral ARVs as prevention. MTN-015 is designed to address these very questions.

**19. What is unique about this study?**

MTN-015 is the first long-term study in women who have acquired HIV during their participation in an HIV prevention trial of a microbicide or oral PrEP. No other research has focused on understanding how the use of microbicides or ARV therapy at the time of infection may alter the natural progression of disease and response to treatment.

**20. When will the study be completed and results known?**

As currently planned, MTN-015 researchers will follow study participants until 2013. Long-term results cannot be expected until this time, although researchers are likely to report preliminary observations periodically during the course of study.

More information about the Microbicide Trials Network and MTN-015 are available at [www.mtnstopshiv.org](http://www.mtnstopshiv.org).

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